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(54) **APPARATUS, METHOD AND SYSTEM FOR PERFORMING PHASE-RESOLVED OPTICAL FREQUENCY DOMAIN IMAGING**

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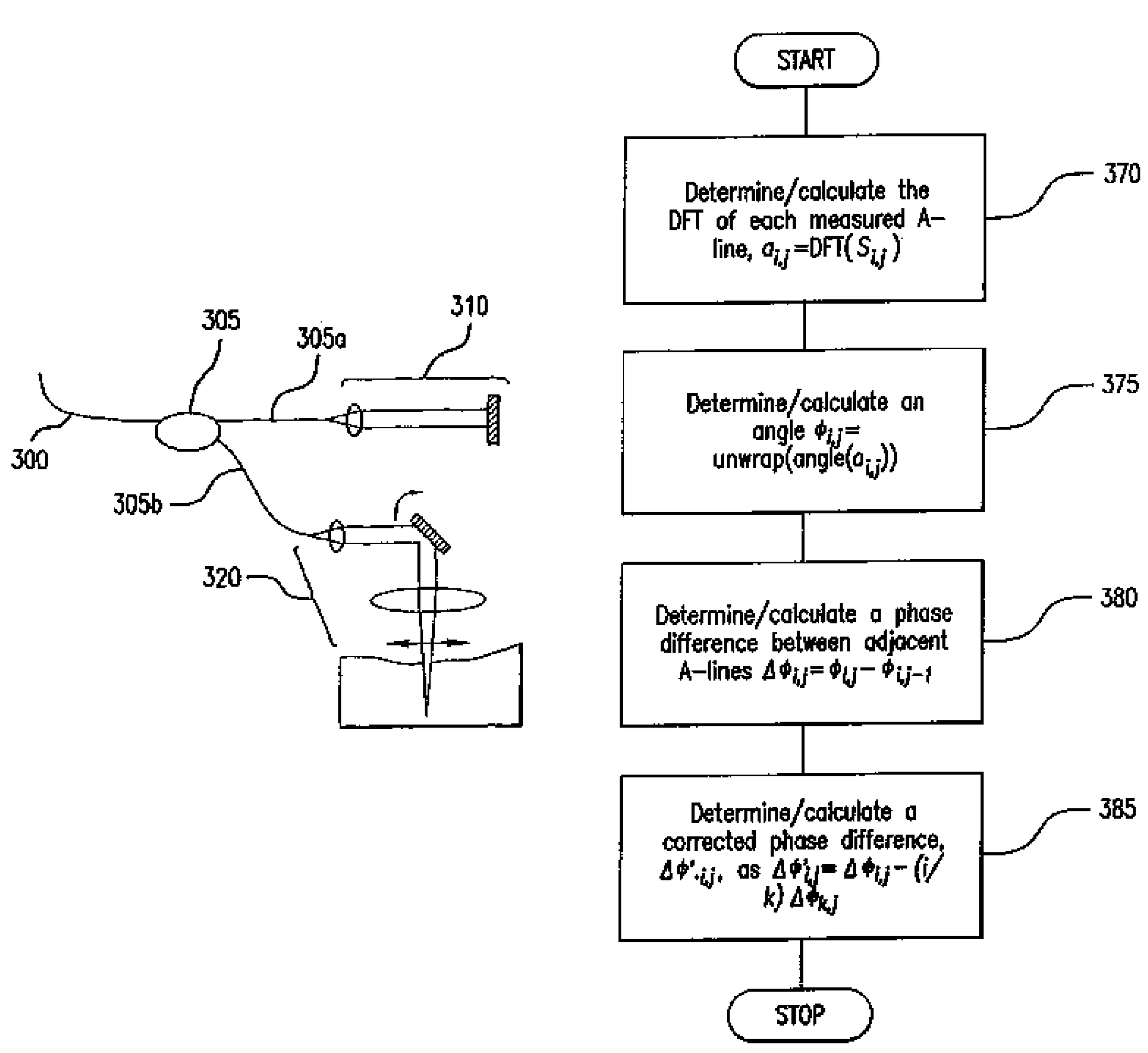
(57) **ABSTRACT**

Apparatus, system and method are provided which utilize signals received from a reference and a sample. In particular, a radiation is provided which includes at least one first electro-magnetic radiation directed to the sample and at least one second electro-magnetic radiation directed to the reference. A frequency of the radiation varies over time. An interference can be detected between at least one third radiation associated with the first radiation and at least one fourth radiation associated with the second radiation. It is possible to obtain a particular signal associated with at least one phase of at least one frequency component of the interference, and compare the particular signal to at least one particular information. Further, it is possible to receive at least one portion of the radiation and provide a further radiation, such that the particular signal can be calibrated based on the further signal.

35 Claims, 15 Drawing Sheets



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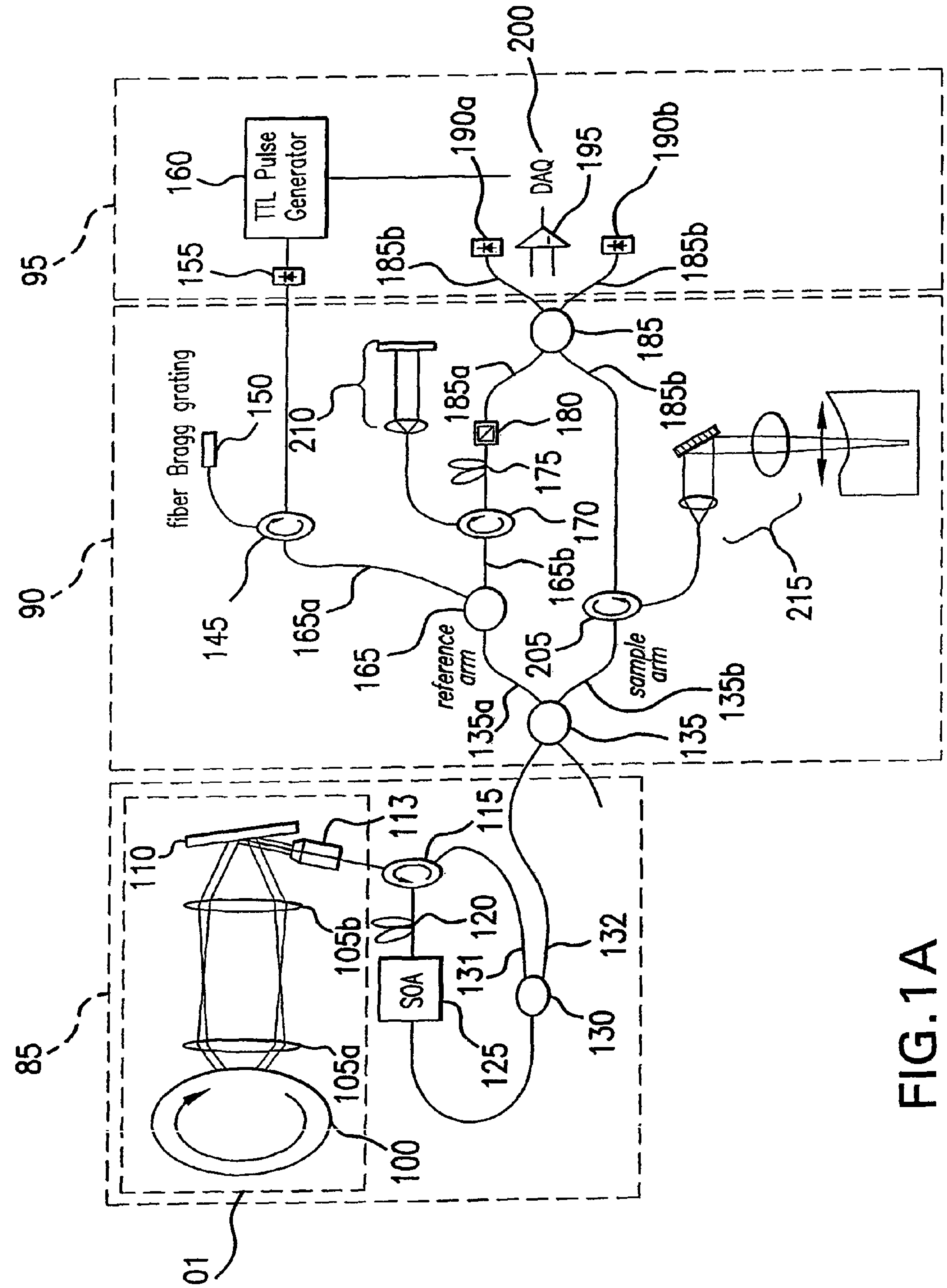


85
90
95
100
101
105a
105b
110
113
115
120
SOA
125
130
131
132
135
135a
135b
reference arm
sample arm
145
fiber Bragg grating
150
155
TTL Pulse Generator
160
165
165a
165b
170
175
180
185
185a
185b
190a
190b
195
DAQ
200
205
210
215

FIG.1A

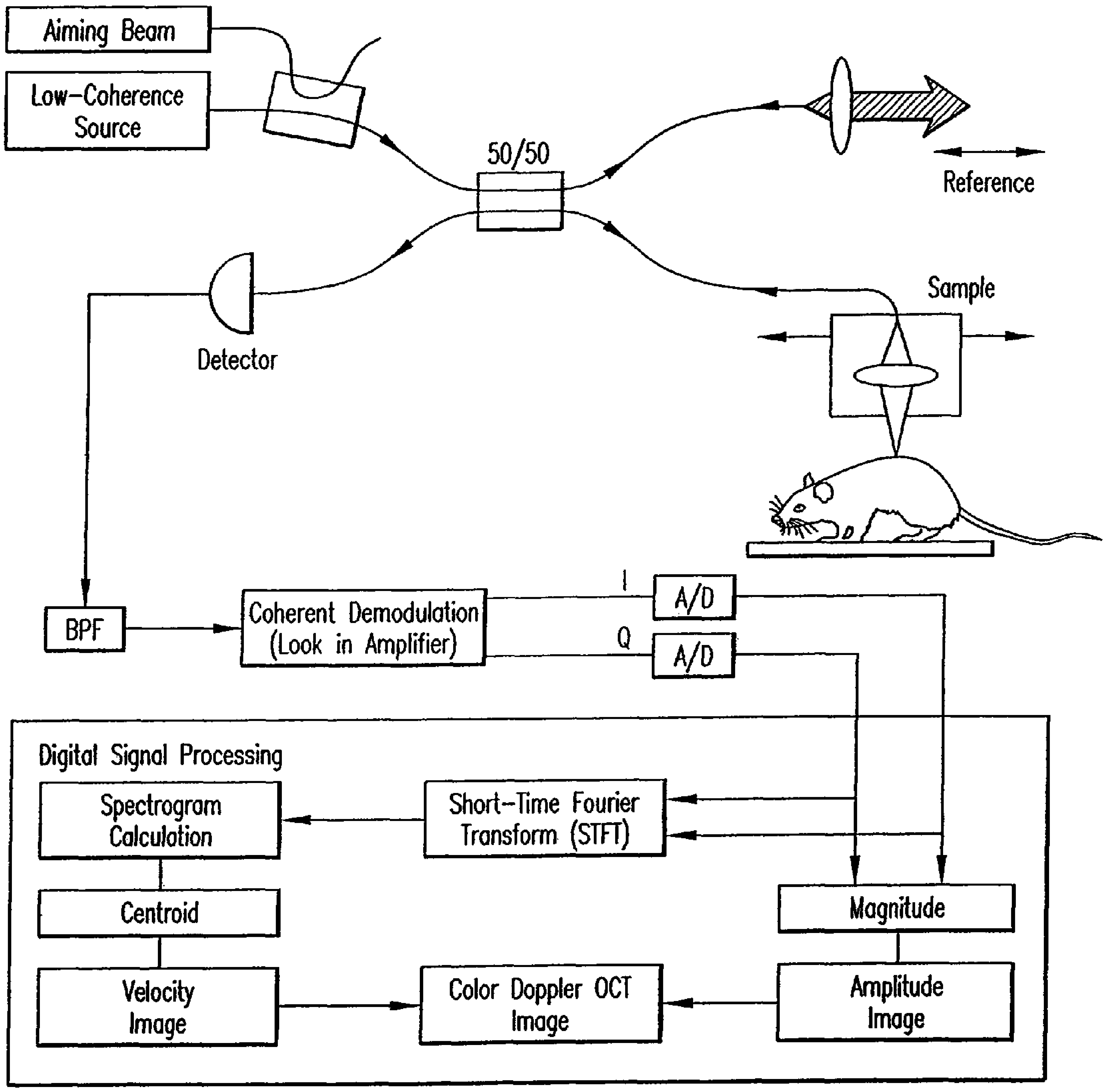


FIG. 1B
PRIOR ART

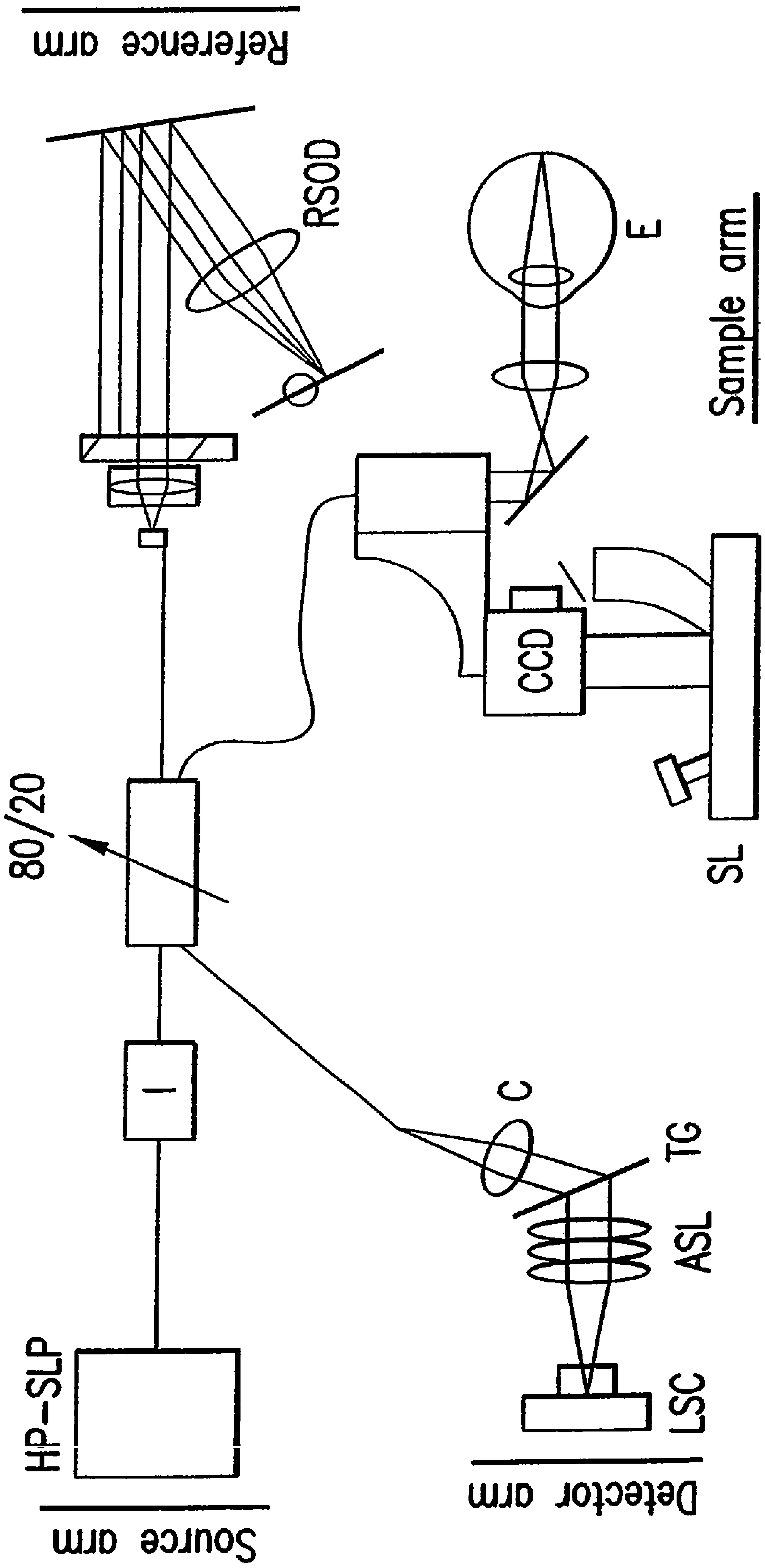
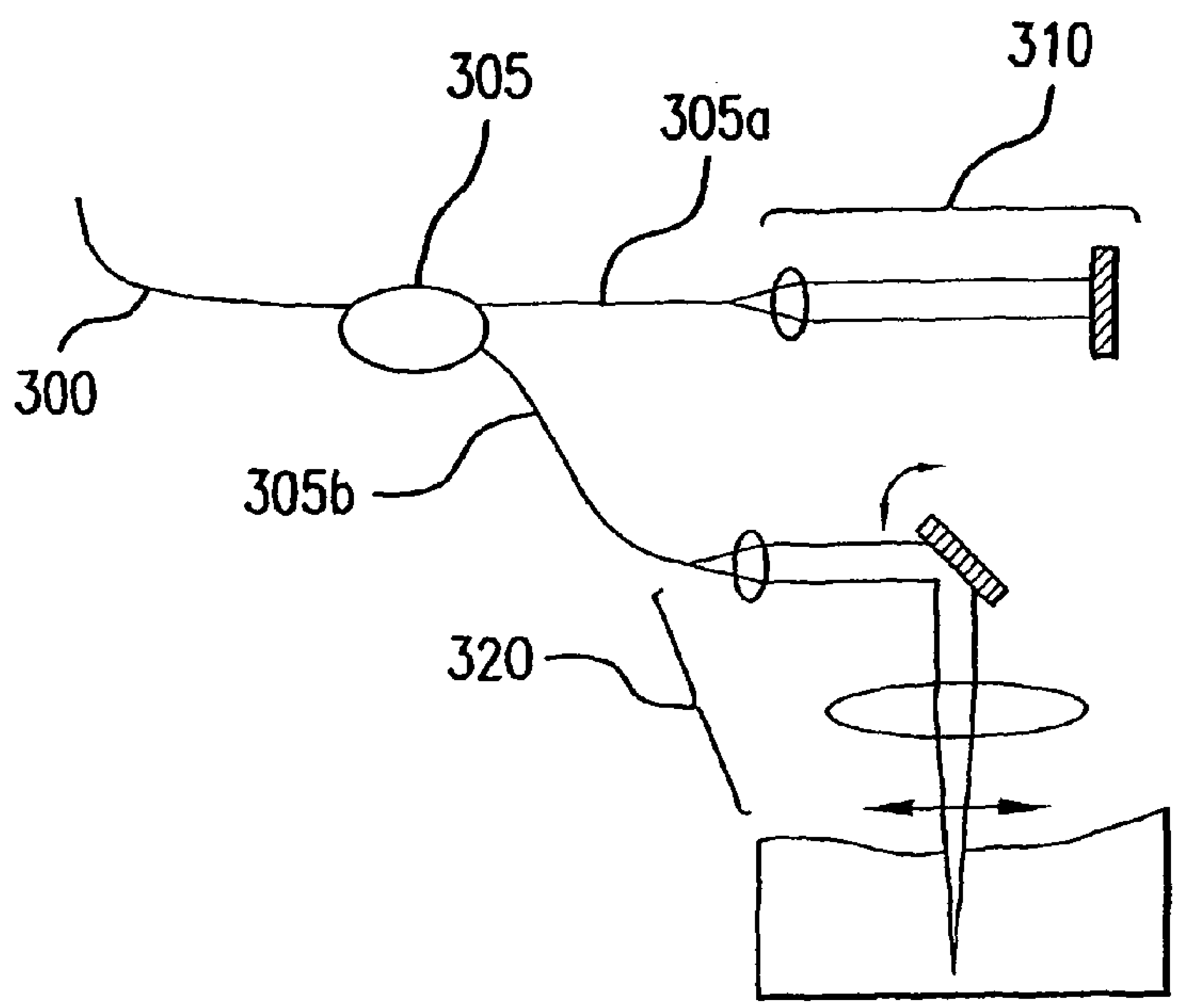
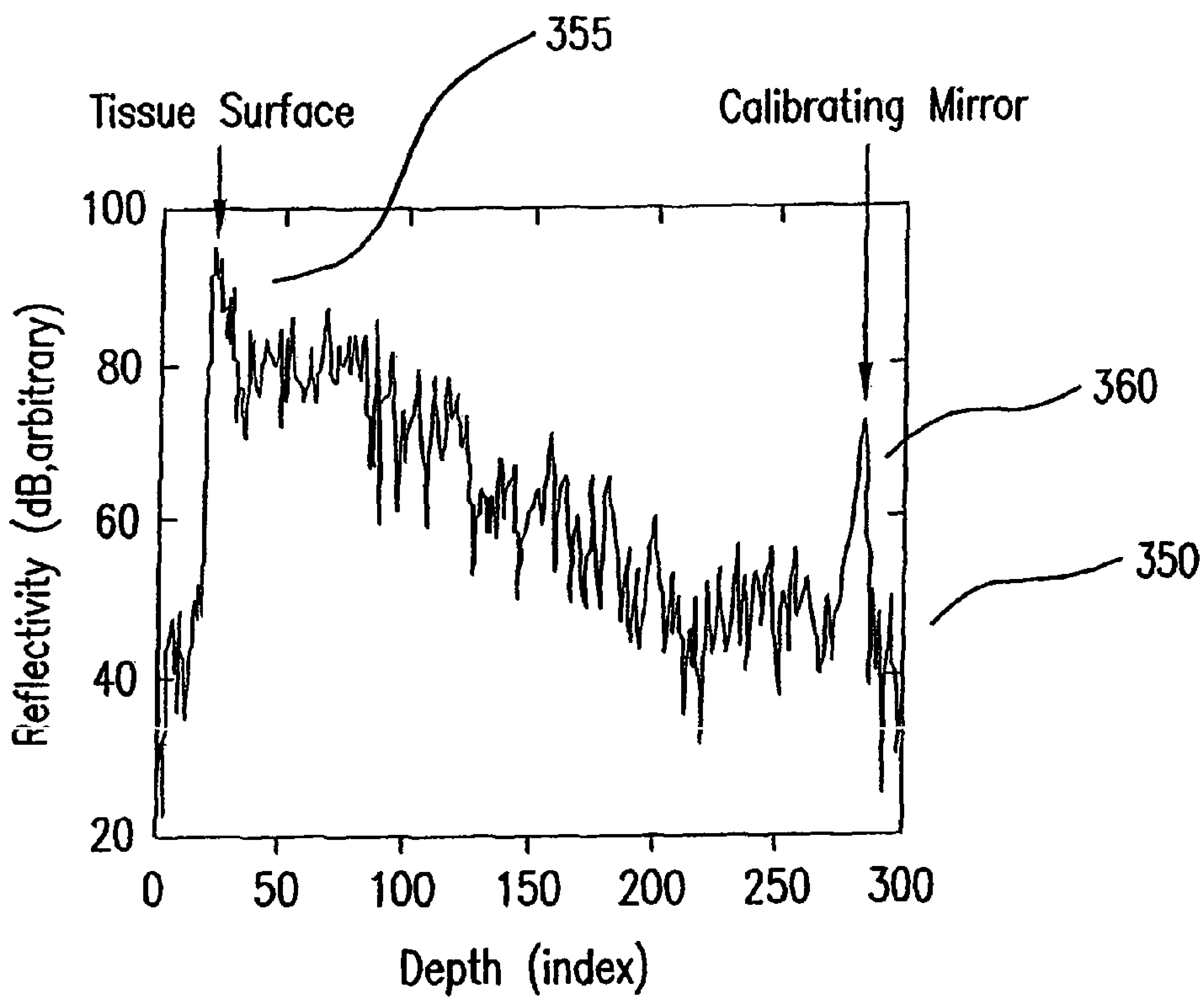


FIG. 1C
PRIOR ART



305
305a
310
300
305b
320

FIG.2



355
Tissue Surface
Calibrating Mirror
100
80
60
40
20
Reflectivity (dB,arbitrary)
360
350
0
50
100
150
200
250
300
Depth (index)

FIG.3A

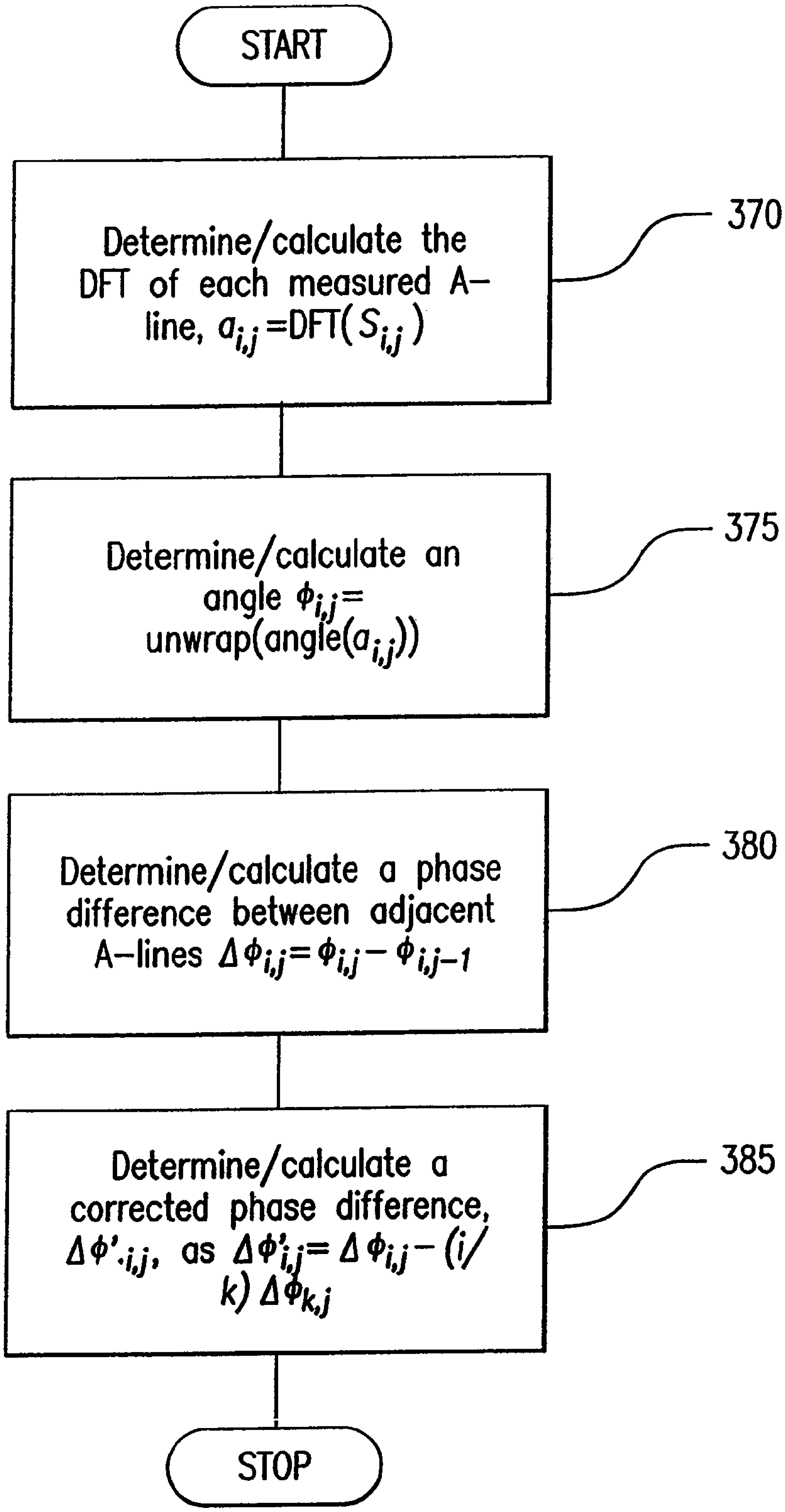

START
Determine/calculate the DFT of each measured A-line, $a_{i,j}$=DFT($S_{i,j}$)
370
Determine/calculate an angle $\phi_{i,j}$= unwrap(angle($a_{i,j}$))
375
Determine/calculate a phase difference between adjacent A-lines $\Delta\phi_{i,j}=\phi_{i,j}-\phi_{i,j-1}$
380
Determine/calculate a corrected phase difference, $\Delta\phi'_{\cdot i,j}$, as $\Delta\phi'_{i,j}=\Delta\phi_{i,j}-(i/k)\Delta\phi_{k,j}$
385
STOP

FIG.3B

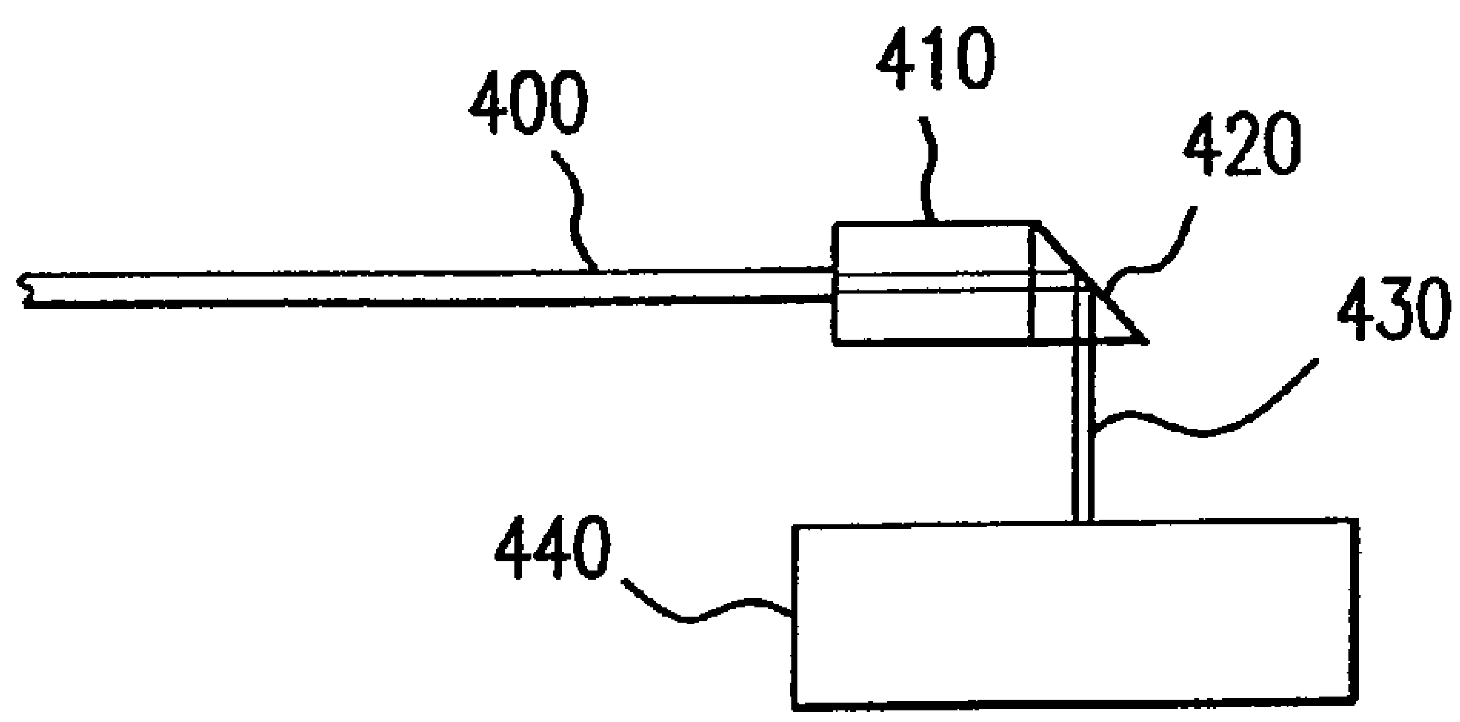


FIG.4
PRIOR ART

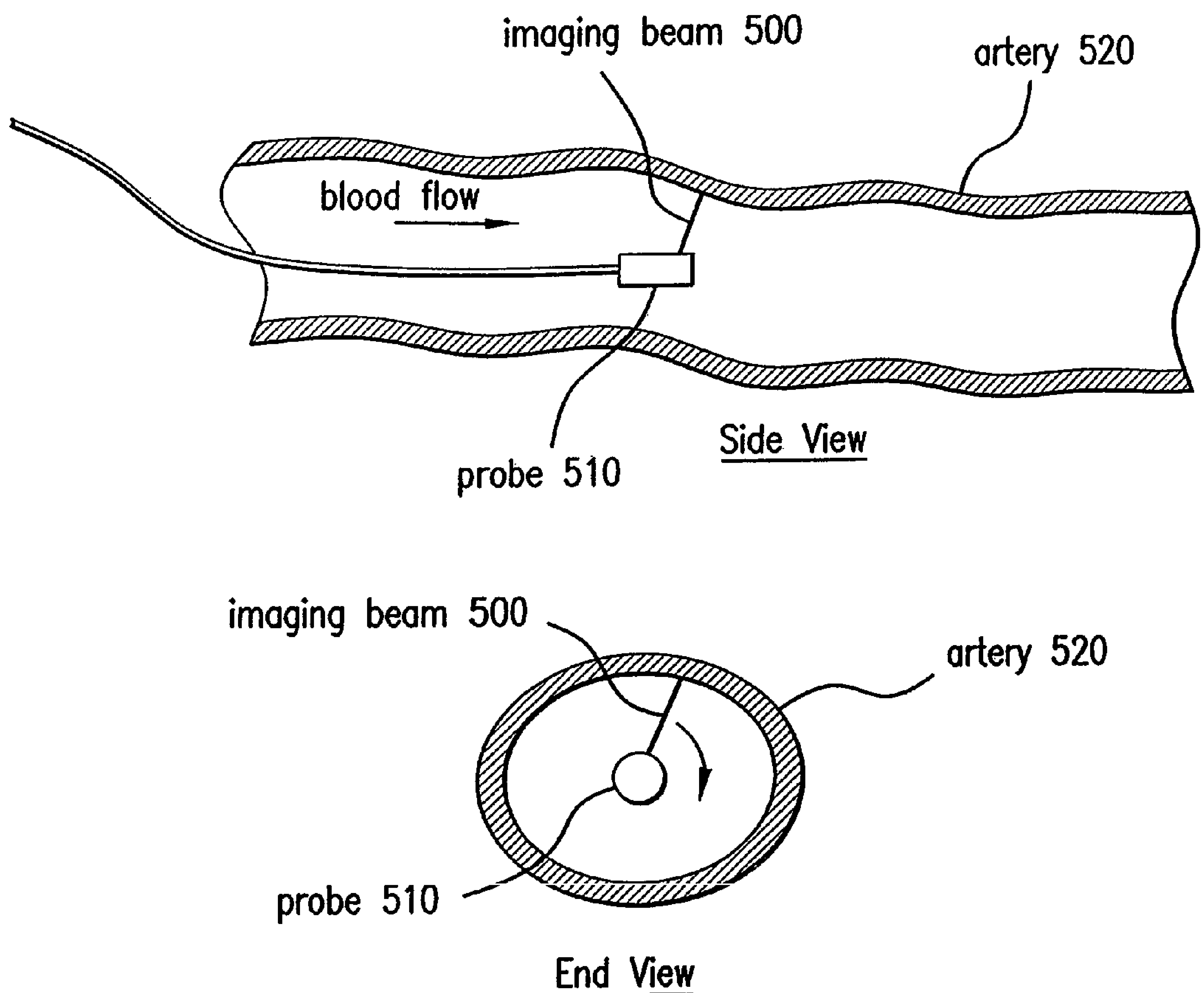
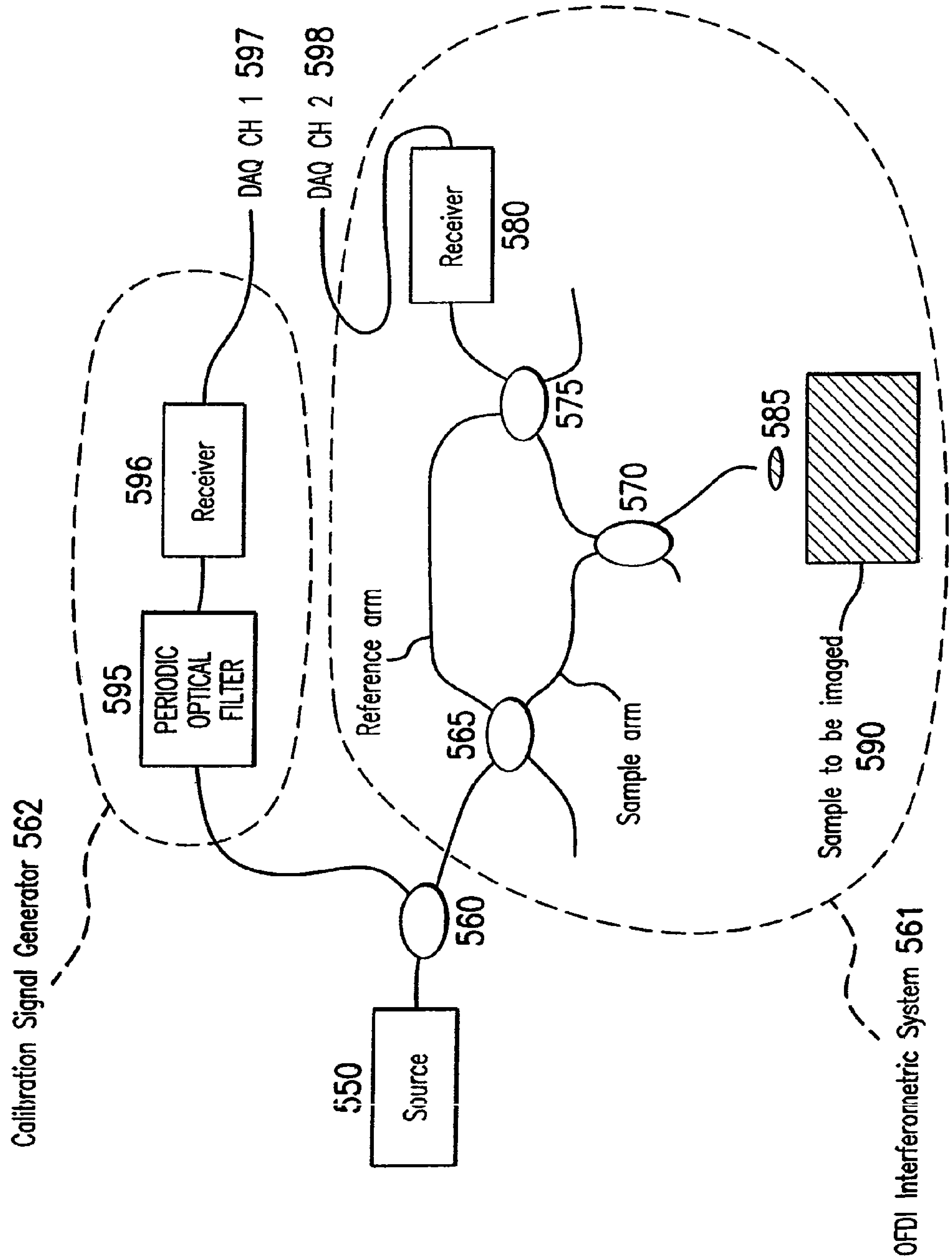


FIG.5



Calibration Signal Generator 562
550
Source
560
595
PERIODIC OPTICAL FILTER
596
Receiver
DAQ CH 1 597
DAQ CH 2 598
Receiver
580
575
565
Reference arm
Sample arm
570
585
Sample to be imaged
590
OFDI Interferometric System 561

FIG.6

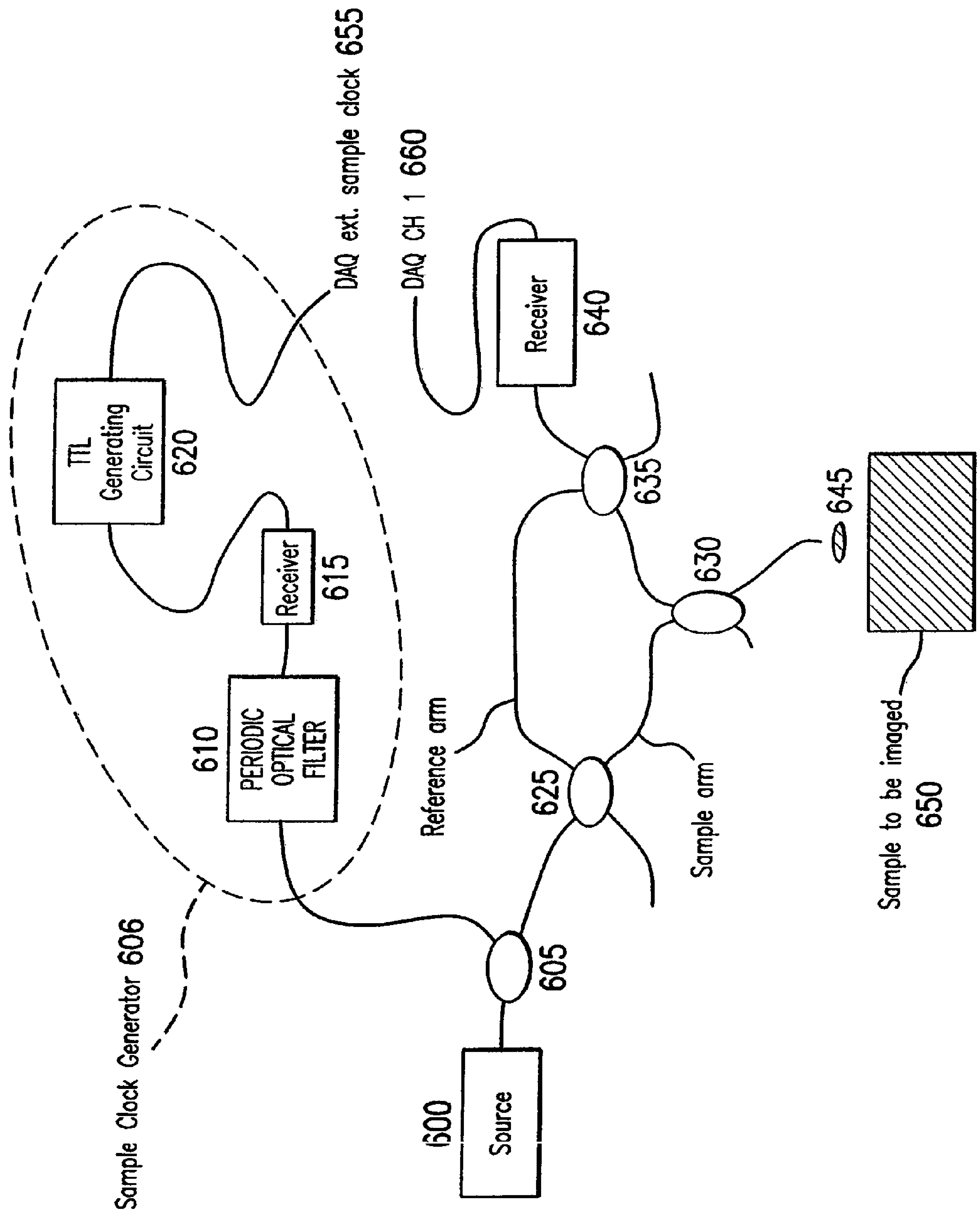

Sample Clock Generator 606
DAQ ext. sample clock 655
DAQ CH 1 660
TTL Generating Circuit
620
Receiver
615
PERIODIC OPTICAL FILTER
610
Receiver
640
635
630
645
Reference arm
625
Sample arm
605
Source
600
Sample to be imaged
650

FIG. 7

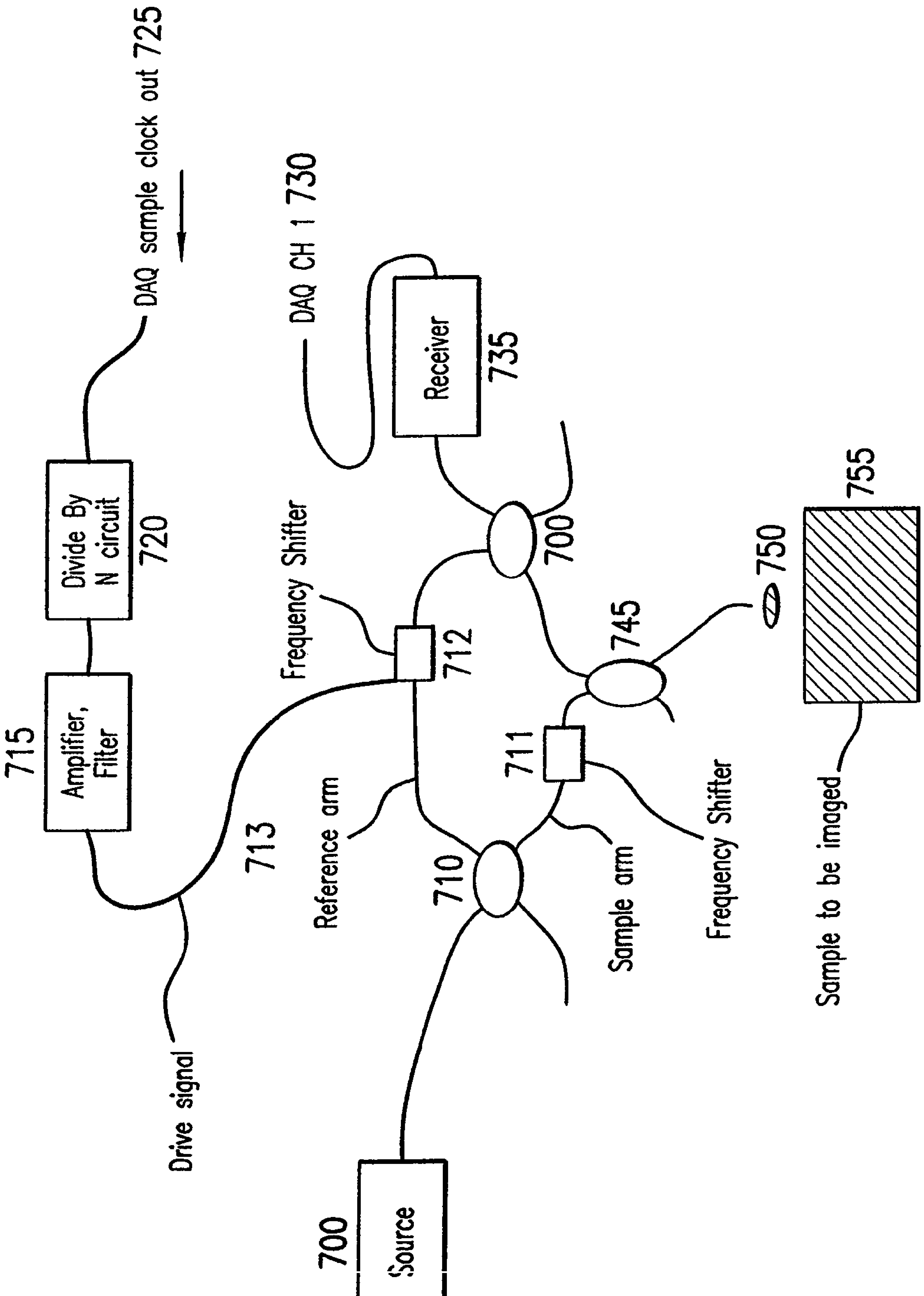

DAQ sample clock out 725
DAQ CH 1 730
Receiver
735
Divide By N circuit
720
Amplifier, Filter
715
Frequency Shifter
712
700
745
750
755
713
Reference arm
711
710
Sample arm
Frequency Shifter
Sample to be imaged
Drive signal
700
Source

FIG.8

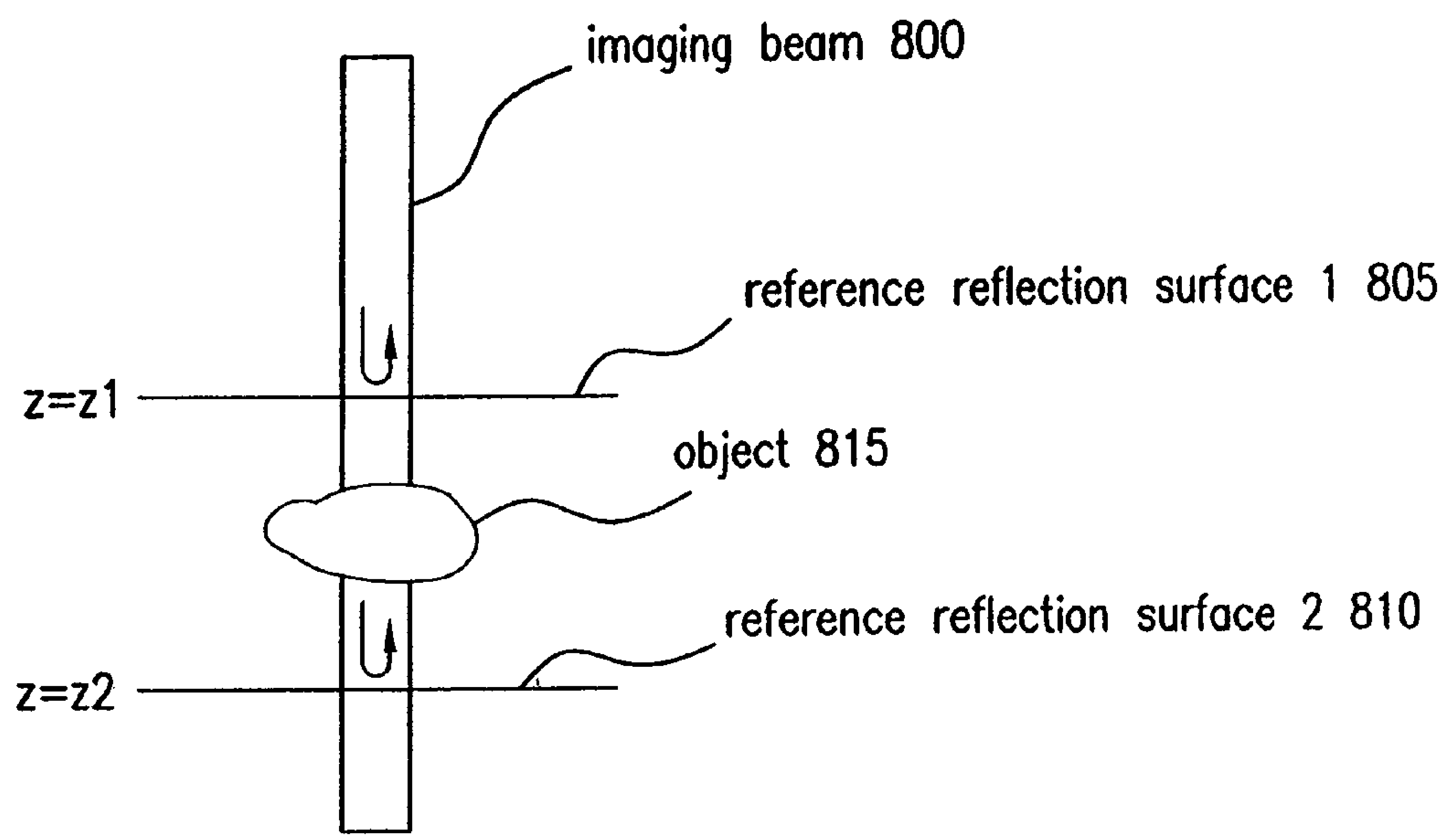

imaging beam 800
reference reflection surface 1 805
z=z1
object 815
reference reflection surface 2 810
z=z2

FIG.9

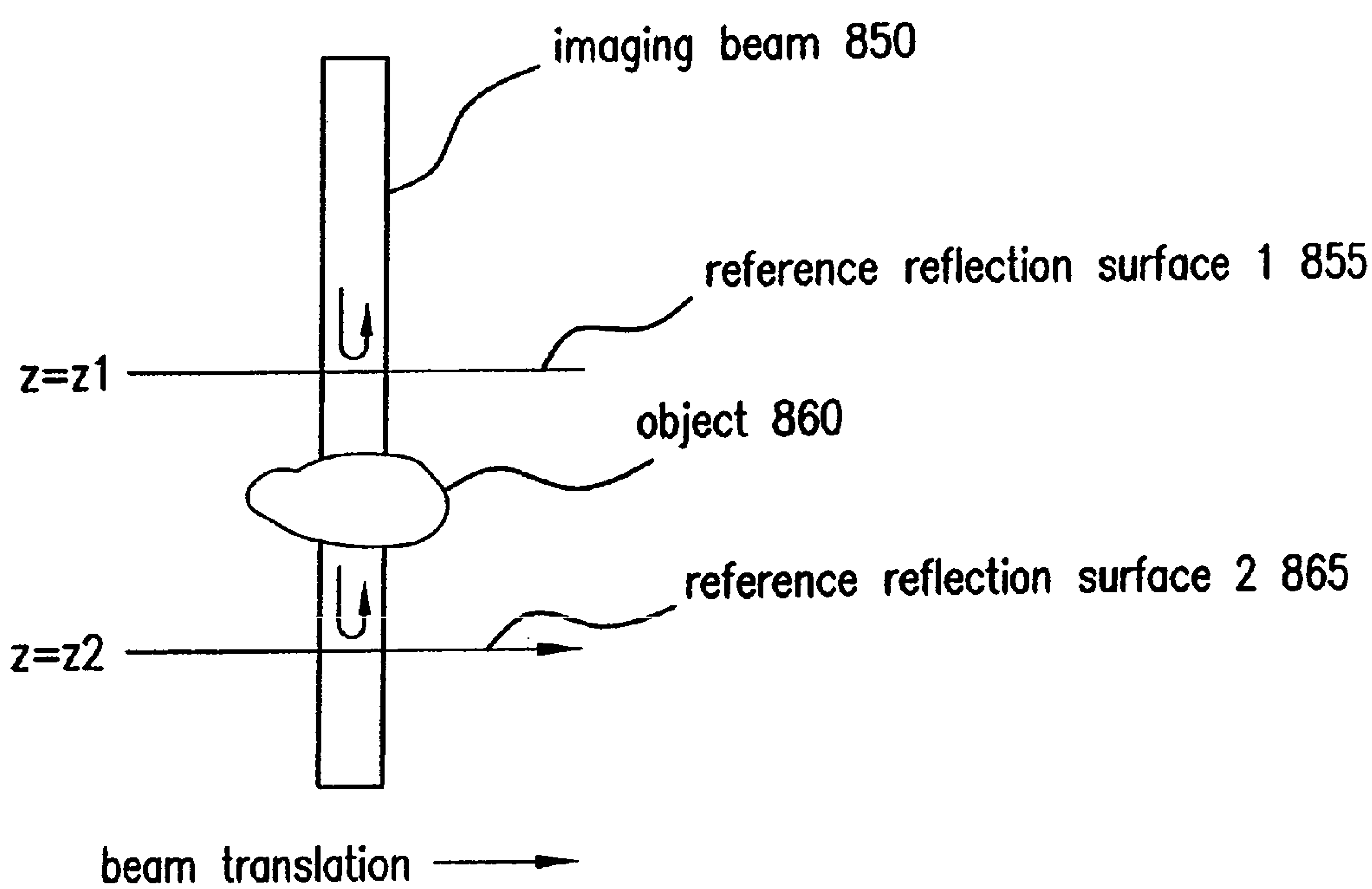

imaging beam 850
reference reflection surface 1 855
z=z1
object 860
reference reflection surface 2 865
z=z2
beam translation

FIG.10

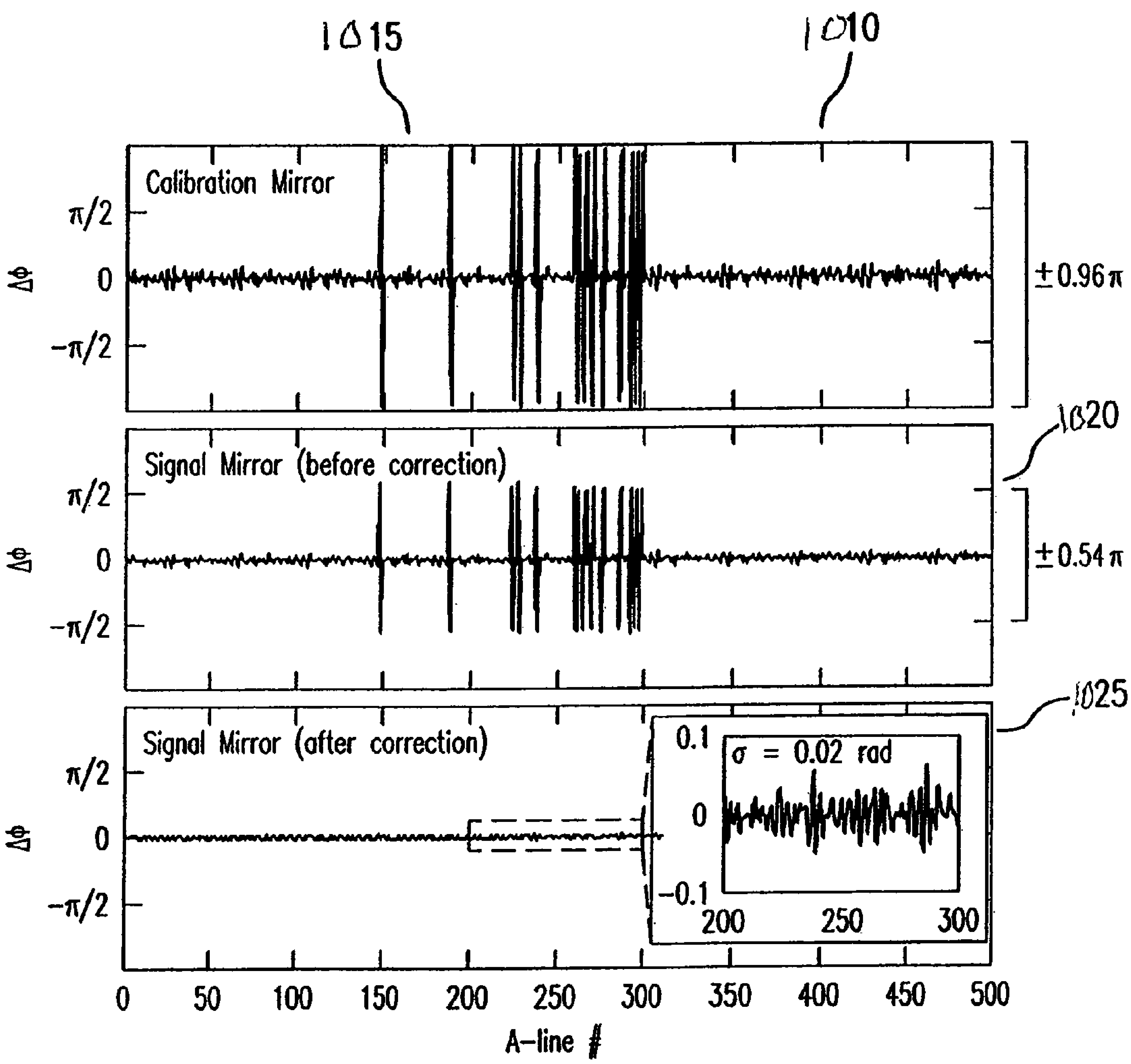

1015
1010
Calibration Mirror
π/2
Δφ
0
−π/2
±0.96π
1020
Signal Mirror (before correction)
±0.54π
1025
Signal Mirror (after correction)
0.1
σ = 0.02 rad
−0.1
200
250
300
0 50 100 150 200 250 300 350 400 450 500
A-line #

FIG.11

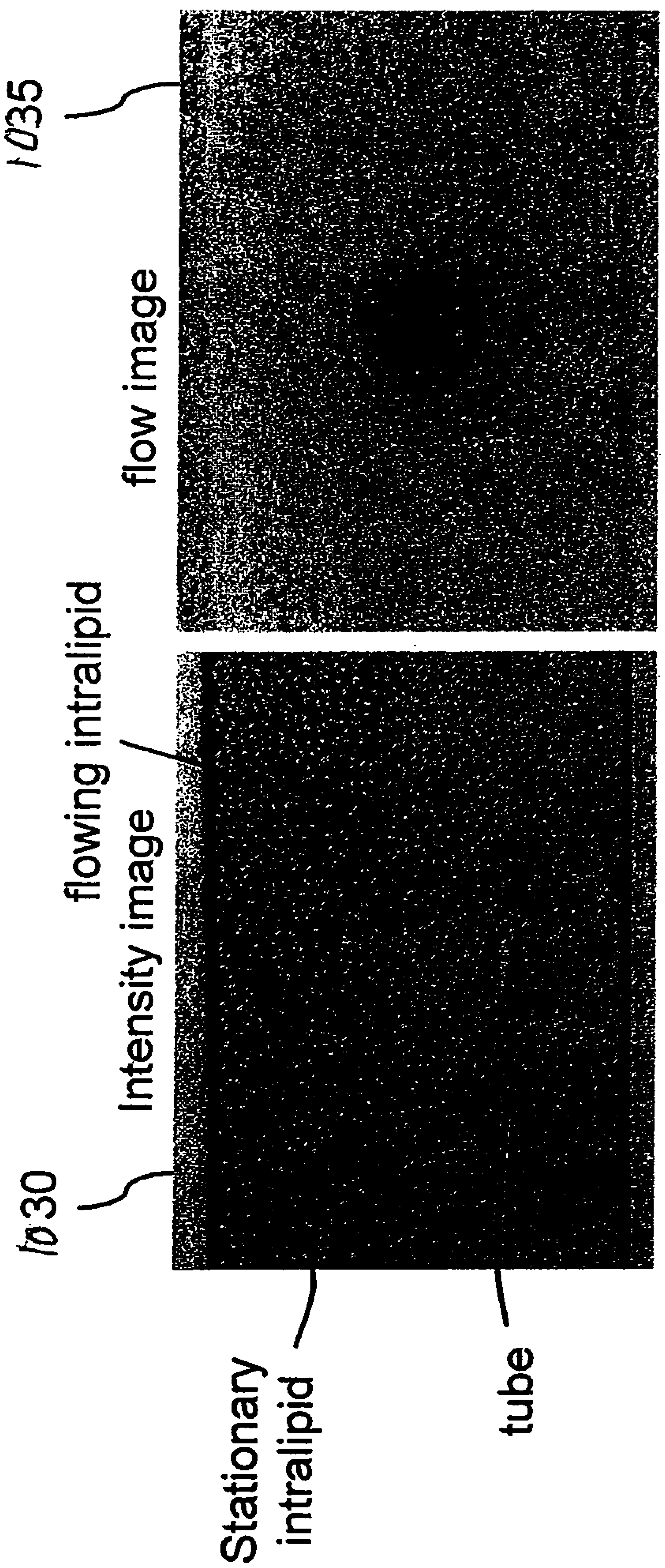

1035
flow image
1030
Intensity image
flowing intralipid
Stationary intralipid
tube

FIG. 12

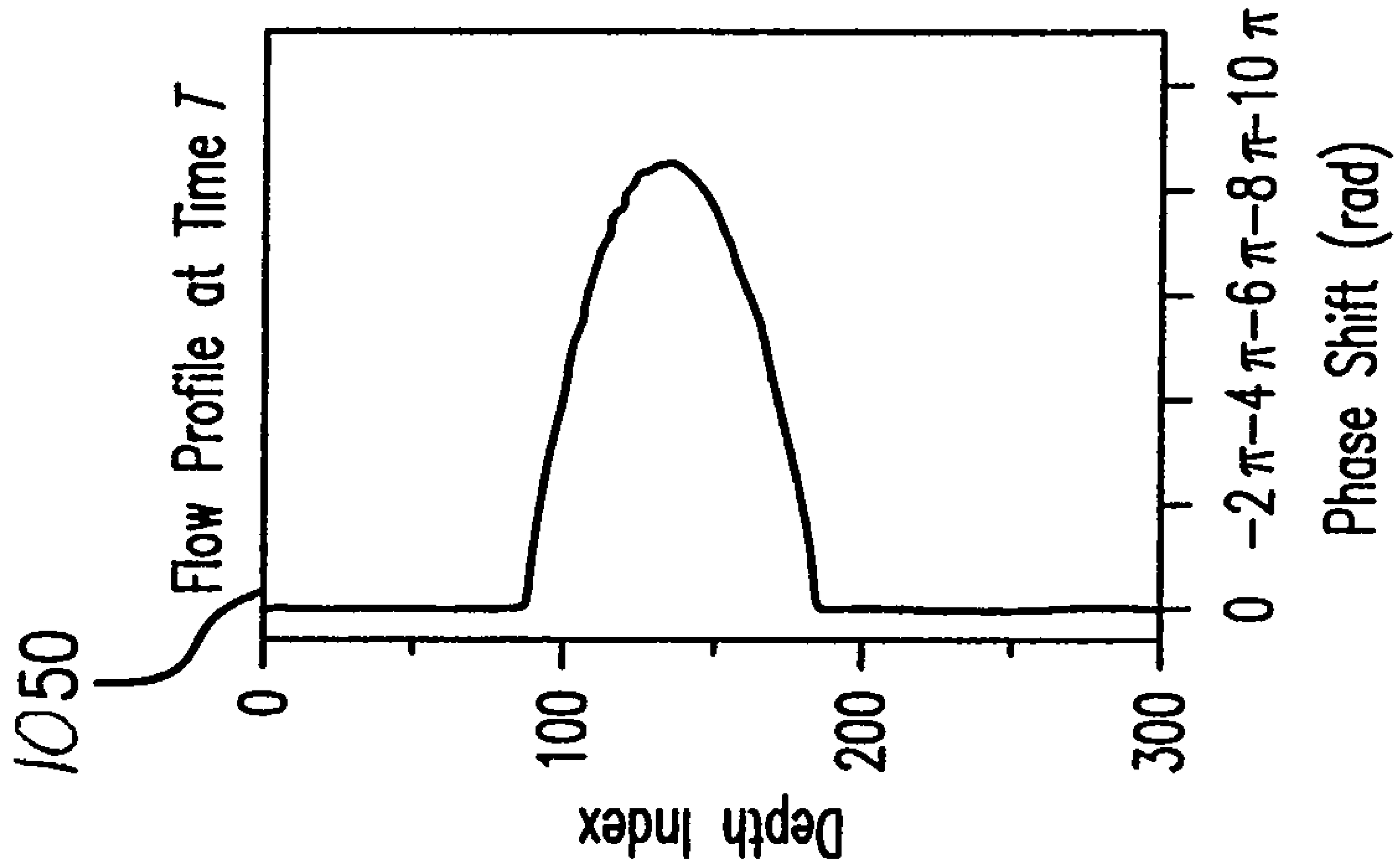


FIG.13C

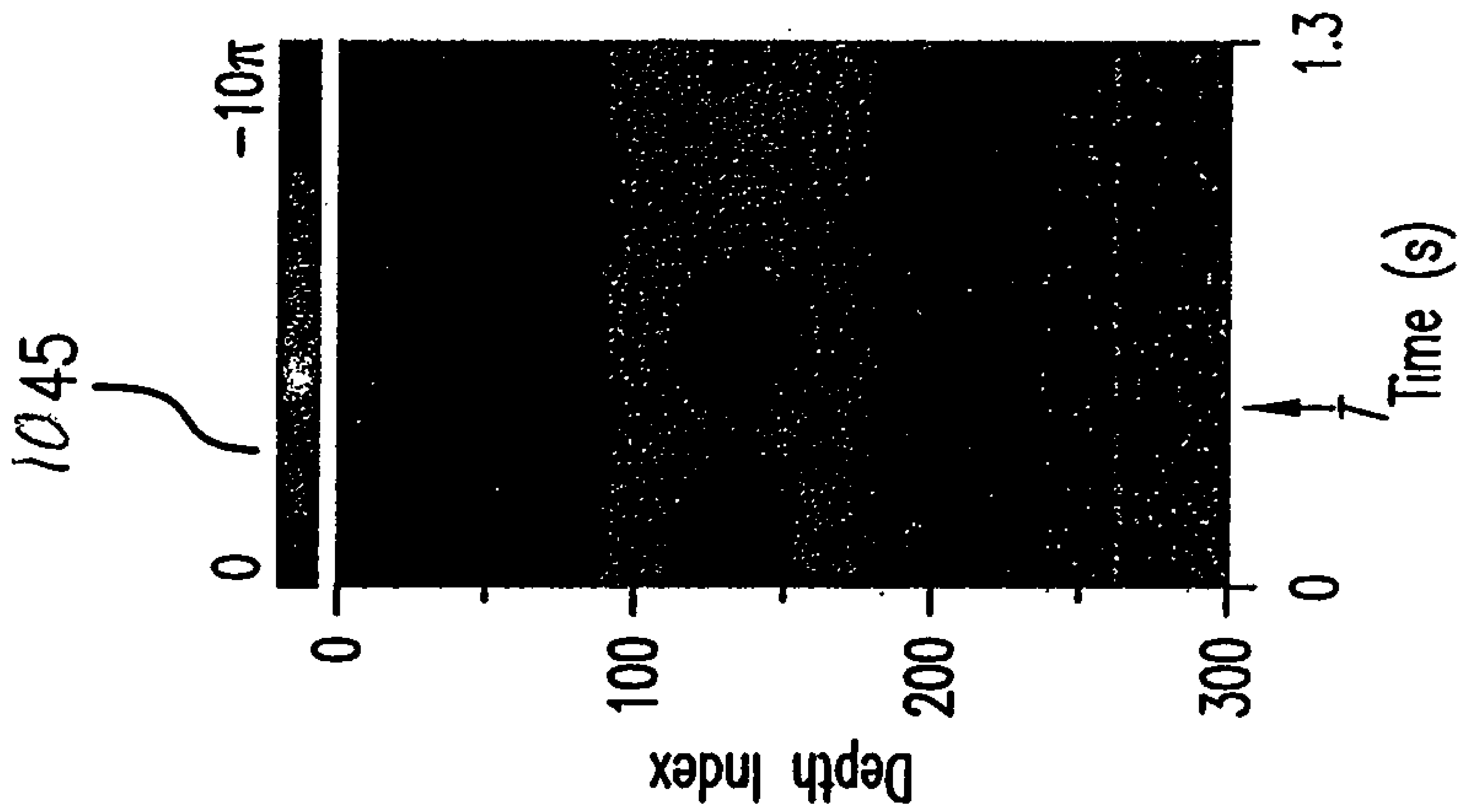


FIG.13B

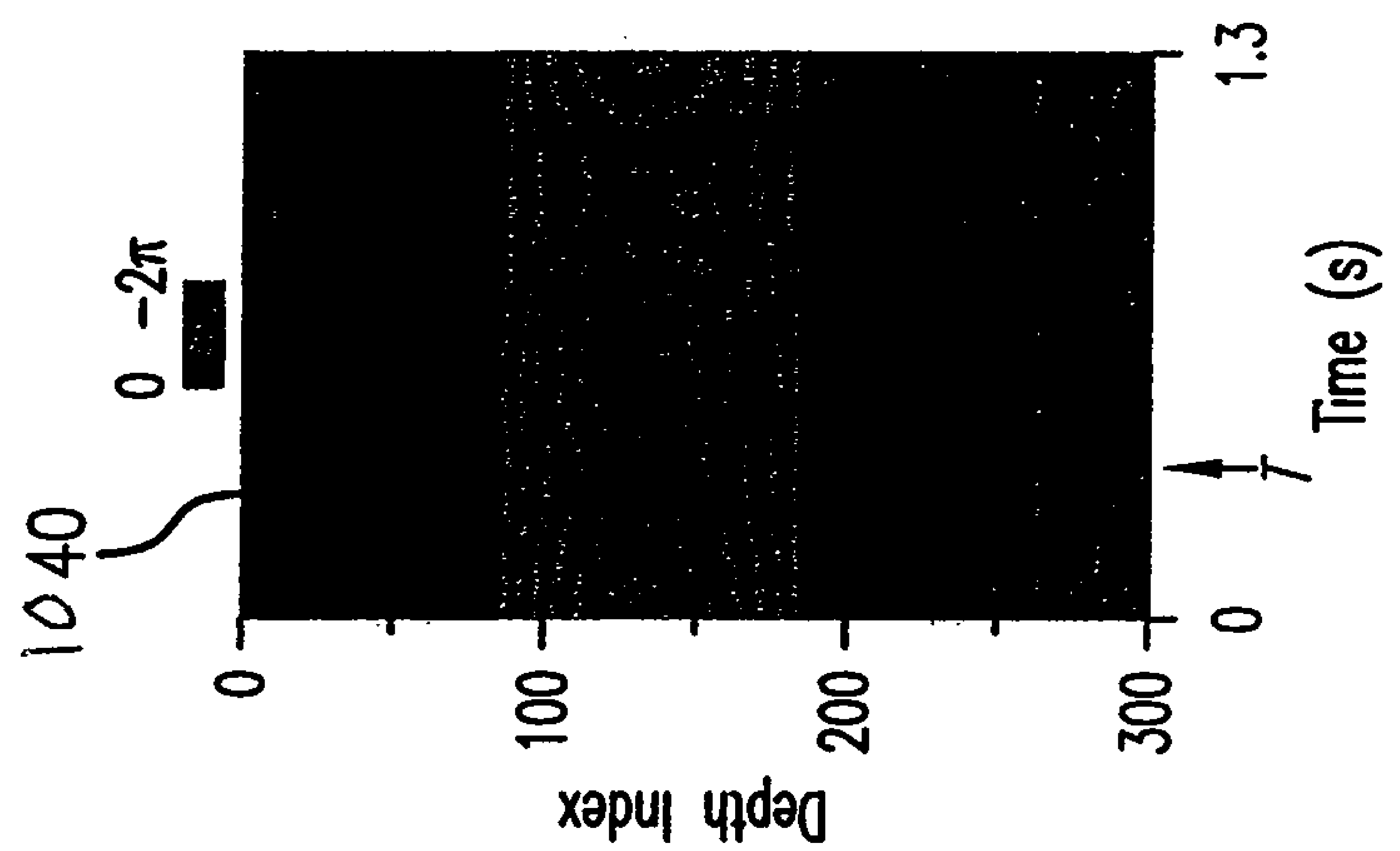
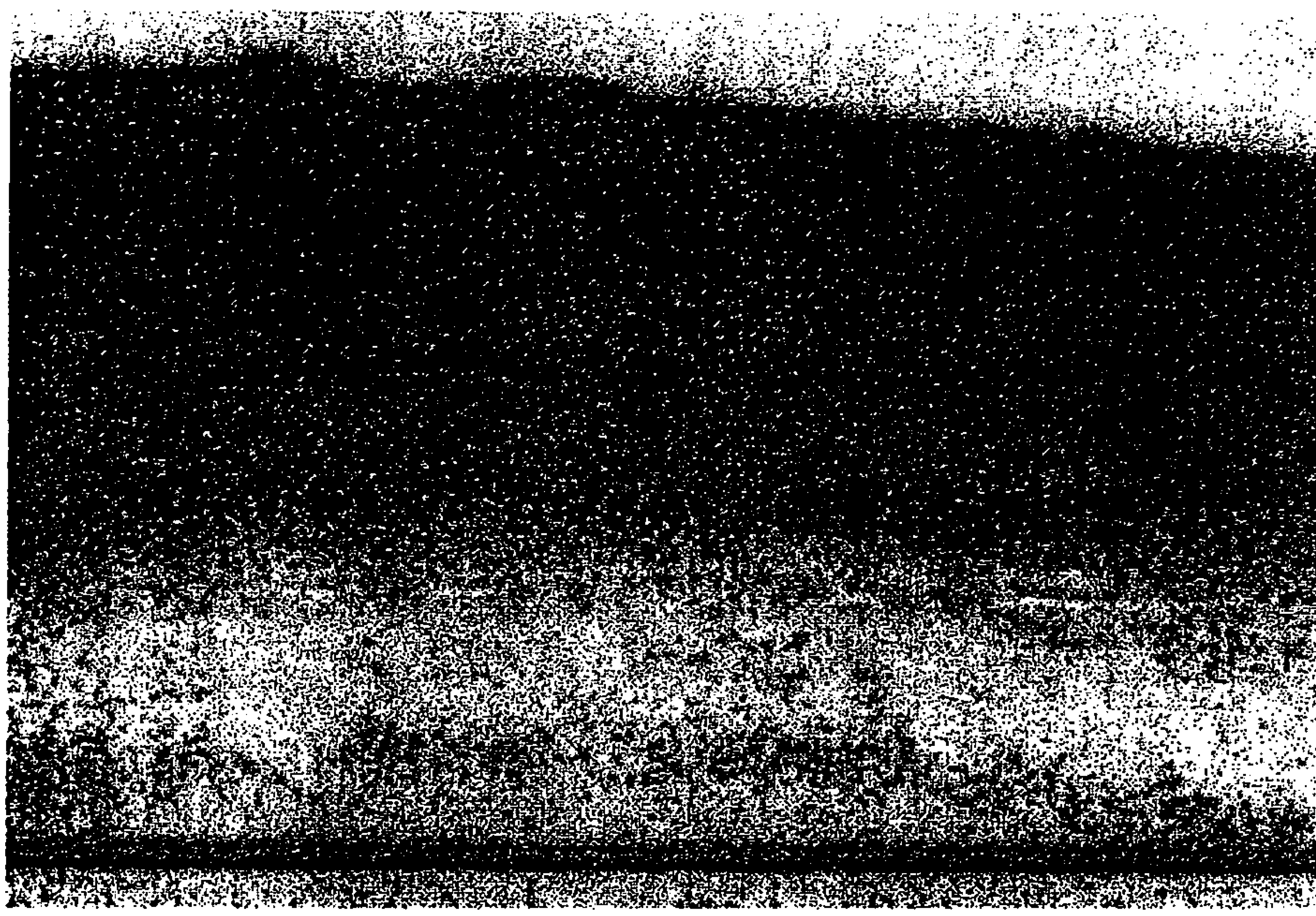


FIG.13A

360

intensity image



1055

flow image

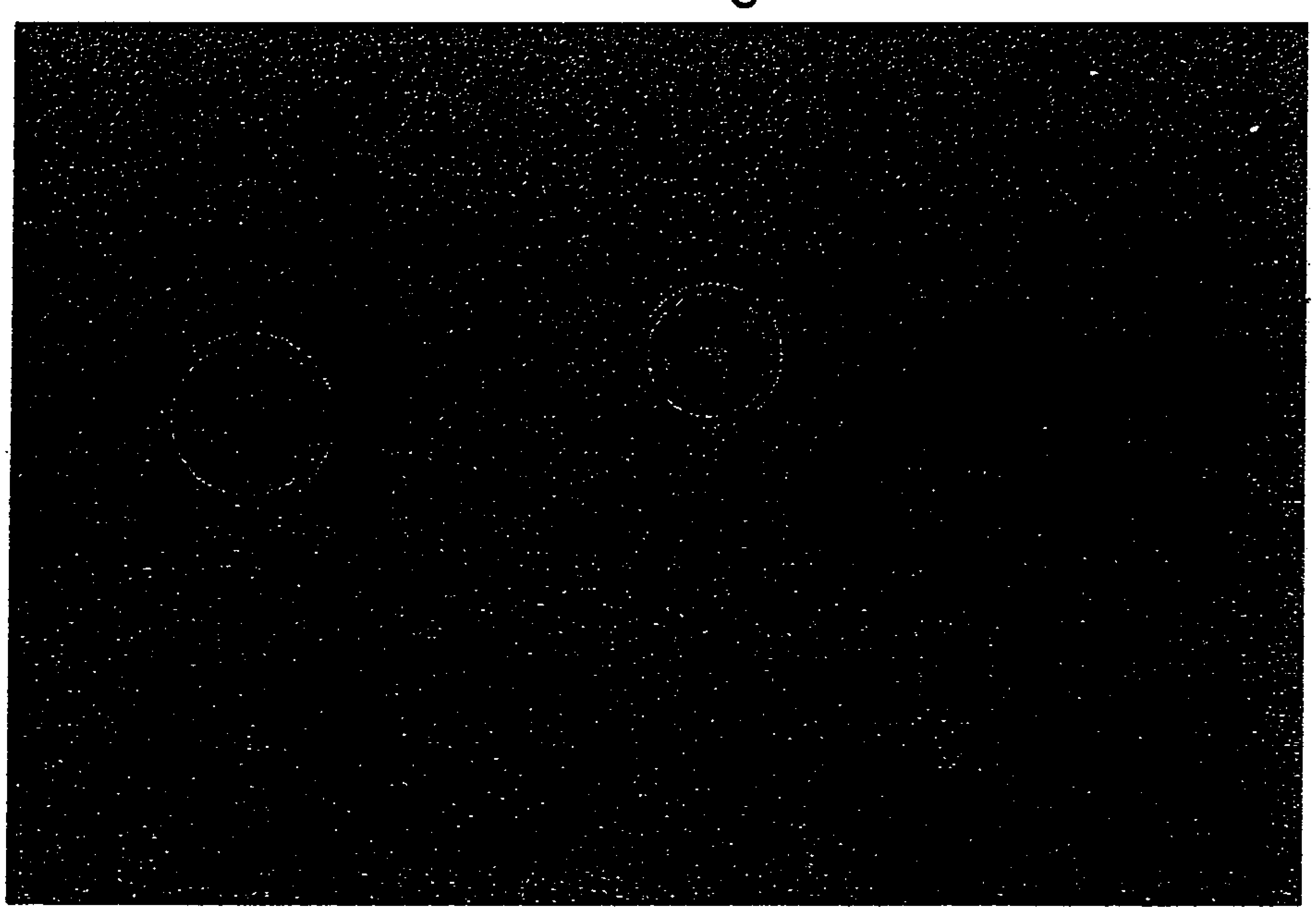


FIG. 14

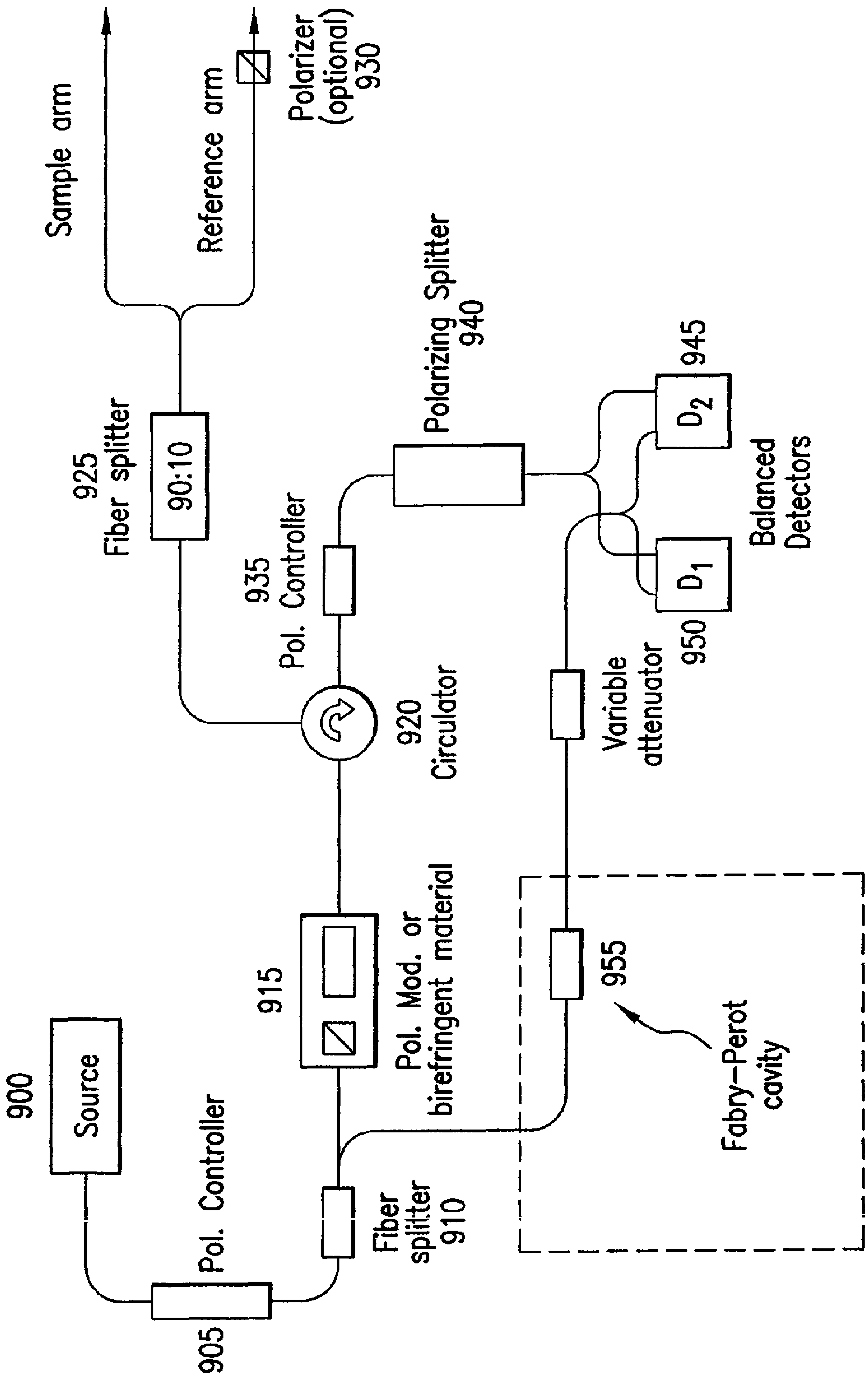

Sample arm
Reference arm
Polarizer (optional) 930
925 Fiber splitter
90:10
935 Pol. Controller
Polarizing Splitter 940
945
D2
D1
950
Balanced Detectors
920 Circulator
Variable attenuator
915
Pol. Mod. or birefringent material
955
Fabry–Perot cavity
900
Source
Pol. Controller
905
Fiber splitter 910

FIG. 15

APPARATUS, METHOD AND SYSTEM FOR PERFORMING PHASE-RESOLVED OPTICAL FREQUENCY DOMAIN IMAGING

CROSS-REFERENCE TO RELATED APPLICATION(S)

This application is based upon and claims the benefit of priority from U.S. patent application Ser. No. 60/686,790, filed Jun. 1, 2005, the entire disclosure of which is incorporated herein by reference.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH

The research leading to the present invention was supported, at least in part, by National Institute of Health, Grant numbers R33 CA110130 and R01 HL70039. Thus, the U.S. government may have certain rights in the invention.

FIELD OF THE INVENTION

The present invention relates to apparatus, method and system for imaging at least a portion of a sample in n optical frequency domain, and more particularly for performing phase-resolved imaging of transparent and turbid samples using optical frequency domain imaging techniques.

BACKGROUND INFORMATION

Optical coherence tomography ("OCT") is an imaging technique that measures the interference between a reference beam of light and a beam reflected back from a sample. A detailed system description of traditional time-domain OCT was first described in Huang et al. "Optical Coherence Tomography," Science 254, 1178 (1991). Detailed system descriptions for spectral-domain OCT and Optical Frequency Domain Interferometry are given in International Patent Application No. PCT/US03/02349 and U.S. patent application No. 60/514,769, respectively. Polarization-sensitive OCT provides additional contrast by observing changes in the polarization state of reflected light. The first fiber-based implementation of polarization-sensitive time-domain OCT was described in Saxer et al., "High-speed fiber-based polarization-sensitive optical coherence tomography of in vivo human skin," Opt. Lett. 25, 1355 (2000).

In one exemplary technique of OCT, cross-sectional images of biological samples can be provided with a resolution on the scale of several to tens of microns. Contrast in the conventional OCT techniques can result from differences in the optical scattering properties of various tissues, and may permit imaging of tissue microstructures. Additional biological or functional information can be obtained by applying Doppler techniques to measure spatially-localized motion in the sample. These exemplary techniques, which can be referred to as Color Doppler OCT or Optical Doppler Tomography, have been used for imaging blood flow in skin, retina, esophagus, etc. Simultaneous imaging of tissue microstructure and blood flow can significantly enhance the diagnostic utility of OCT. Initial Doppler OCT measurements were performed with time-domain OCT (TD-OCT) systems, an example of which is shown in FIG. 1B.

Recently, it has been demonstrated that Fourier-Domain OCT (FD-OCT) provides significantly improved sensitivity, enabling high-speed imaging. FD-OCT has been implemented in two configurations, spectral-domain OCT ("SD-OCT") and optical frequency domain imaging ("OFDI"). In SD-OCT, a spectrometer is used to record spectral fringes that result from the interference of a reference beam with light reflected from a sample. In OFDI, a narrowband wavelength-swept source and a single detector are used to record the same interferogram. Doppler imaging has been demonstrated recently in SD-OCT systems. An example of a Doppler SD-OCT system is shown in FIG. 1C. Doppler imaging using OFDI technique has not been demonstrated to our knowledge. OFDI procedure, however, may become the preferred imaging modality for several applications since it is less prone to motion artifacts associated with endoscopy and can provide a significantly larger depth range. Continued development of wavelength-swept laser sources promises further improvements in imaging speed and resolution. These advantages are compelling in several OCT applications, including Barrett's esophagus screening and coronary imaging. As such, flow imaging in many applications may require the development of phase-resolved OFDI.

Convention OCT systems and techniques create images based on the magnitude of the reflectivity as a function of depth. Additional information can be obtained by examining a phase of the reflectivity of the signal. Typically, a phase information of a signal can be meaningful when compared to another phase of the signal. This phase can be another measurement of the phase at a different depth or a measurement of phase at the same depth from a successive depth scan. Regardless of the exact implementation, the sensitivity of the image constructed from the phase measurements can be a function of the noise on the individual phase measurements and the repeatability of phase measurements.

In phase-resolved Doppler OFDI, it is possible for synchronization errors to induce spurious measurements of the interference fringe phases, resulting in a reduced performance. These synchronization errors can be referred to hereafter as timing-induced phase errors.

OBJECTS AND SUMMARY OF EXEMPLARY EMBODIMENTS

To address and/or overcome the above-described problems and/or deficiencies, exemplary systems, methods and apparatus are provided for reducing the effect of the timing-induced phase errors. For example, in certain conventional methods, additional optical signals are generated and used to measure timing-induced errors so that they can be removed from the measured image. In other techniques, improved synchronization schemes can be presented to reduce the magnitude of the timing-induced phase noise directly.

According to the present invention, exemplary systems, methods and apparatus are provided for facilitating high-sensitivity depth-resolved phase measurements using an exemplary OFDI system. For example, a measurement of the phase can be used to measure blood flow and other motion in a turbid or scattering media, and can also be used to monitor optical thickness of materials over time or as a function of transverse location. Exemplary methods for achieving high-sensitivity in accordance with the exemplary embodiments of the present invention are also described herein. In one such exemplary method, a calibration signals can be generated and utilized to correct, modify and/or otherwise address timing-induced phase measurement errors. According to another exemplary embodiment of the present invention, the exemplary OFDI system may be modified to allow a simultaneous measurement of a calibration signal with the sample signal, and can also provide an exemplary procedure for correcting, modifying and/or otherwise addressing timing-induced phase measurements in the sample signal, e.g., by using such calibration signal. In still another exemplary embodiment of the present invention, the calibration signal can be generated on a separate channel and acquired independently of the sample signal. For example, the calibration signal can be similarly used to correct errors in the sample signal. Additionally, according to a further exemplary embodiment of the present invention, method, apparatus and system can be provided for reducing, adjusting and/or minimizing timing-induced phase errors.

Thus, in accordance with one exemplary embodiment of the present invention, apparatus, system and method are provided which utilize signals received from a reference and a sample. In particular, a radiation is provided which includes at least one first electro-magnetic radiation directed to the sample and at least one second electro-magnetic radiation directed to the reference. A frequency of the radiation varies over time. An interference can be detected between at least one third radiation associated with the first radiation and at least one fourth radiation associated with the second radiation. It is possible to obtain a particular signal associated with at least one phase of at least one frequency component of the interference, and compare the particular signal to at least one particular information. Further, it is possible to receive at least one portion of the radiation and provide a further radiation, such that the particular signal can be calibrated based on the further signal.

For example, the particular information can include predetermined data. It is also possible to determine a further signal associated with at least one further phase of at least one further frequency component of the interference, and the at least one particular information can be the further signal. It is also possible to determine a further signal associated with at least one further phase of at least one further frequency component of a further interference, the further interference being different from the interference.

In another exemplary embodiment of the present invention, the further interference may be based on the radiation and the second radiation. The interference and the further interference may also be obtained at different times and/or at different locations of the sample. It is further possible to generate a further signal associated with the radiation, such that the particular information can be provided based on the further signal. In addition, it is possible to receive at least one portion of the radiation and provide a further radiation, and the particular signal and/or the particular information may be associated with the further radiation. In addition, it is possible to calibrate the particular signal based on the further signal. The calibration may be based on an actual distance and/or an optical distance between the sample and a particular arrangement. Further, it is possible to calibrate the particular signal based on an actual distance and/or an optical distance between the sample and the particular arrangement.

These and other objects, features and advantages of the present invention will become apparent upon reading the following detailed description of embodiments of the invention, when taken in conjunction with the appended claims.

BRIEF DESCRIPTION OF THE DRAWINGS

Further objects, features and advantages of the invention will become apparent from the following detailed description taken in conjunction with the accompanying figures showing illustrative embodiments of the invention, in which:

FIG. **1**A is a schematic diagram of an exemplary embodiment of an OFDI system in accordance with the present invention;

FIG. **1**B is a schematic diagram of a conventional Doppler TD-OCT system;

FIG. **1**C is a schematic diagram of an exemplary embodiment of a spectral-domain OCT system in accordance with the present invention;

FIG. **2** is a schematic diagram of an exemplary embodiment of a portion of a system according to one exemplary embodiment of the present invention in which a sample arm that is modified to provide a calibration signal for measurement of timing-induced phase errors;

FIG. **3**A is an exemplary graph illustrating a representative A-line resulting from the exemplary sample arm configuration depicted in FIG. **2**;

FIG. **3**B is an exemplary embodiment of a method for correcting the measured phase differences using this calibration mirror signal in accordance with the present invention;

FIG. **4** is an illustration of a distal end of a conventional OFDI probe showing the existing reflections of the distal end optics which can be used as the calibration signal;

FIG. **5** is an exemplary use of a phase-resolved OFDI probe to measure the blood flow in vivo in accordance with an exemplary embodiment of the present invention;

FIG. **6** is a schematic diagram of another exemplary embodiment of an OFDI system in accordance with the present invention in which the calibration signal is generated from an interferometer that is provided external to the OFDI interferometer;

FIG. **7** is a schematic diagram of yet another exemplary embodiment of the phase-resolved OFDI system in accordance with the present invention which can use an optical generation of the sample clock to synchronize the source wavelength-sweep and acquisition electronics;

FIG. **8** is a schematic diagram of still another exemplary embodiment of the phase-resolved OFDI system in accordance with the present invention that incorporates a frequency-shifter which can be driven with a signal derived from the DAQ sample clock;

FIG. **9** is an illustration of an exemplary use of the exemplary embodiment of the phase-resolved OFDI system to measure depth-resolved changes in optical path length as a function of time;

FIG. **10** is an illustration of an exemplary use of the exemplary embodiment of the phase-resolved OFDI system to measure depth-resolved changes in optical path length as a function of transverse displacement;

FIG. **11** is an exemplary graph of measured differential phases for the calibration mirror and a stationary mirror in the sample arm before and after correction for timing-induced phase errors according to an exemplary embodiment of the present invention;

FIG. **12** is an exemplary illustration of intensity and flow images of an Intralipid phantom as measured by the exemplary embodiment of the phase-resolved Doppler OFDI system according to the present invention;

FIGS. **13**A-**13**C are exemplary illustrations of measurements of depth resolved flow in an Intralipid sample at high flow rates such than phase differences greater than π can be induced;

FIG. **14** is an exemplary illustration of measurements of blood flow in a human skin in vivo implemented using the exemplary embodiments of the present invention; and

FIG. **15** is a block diagram of an exemplary embodiment of a system in accordance with the present invention in which the a calibration signal can be generated by a filter external to an interferometer and such signal can be combined with a balanced detection configuration.

Throughout the figures, the same reference numerals and characters, unless otherwise stated, are used to denote like features, elements, components or portions of the illustrated embodiments. Moreover, while the subject invention will now be described in detail with reference to the figures, it is done so in connection with the illustrative embodiments. It is intended that changes and modifications can be made to the described embodiments without departing from the true scope and spirit of the subject invention as defined by the appended claims.

DETAILED DESCRIPTION OF EXEMPLARY EMBODIMENTS

It should be understood that the exemplary embodiments of systems, software arrangements and methods in accordance with the present invention can be implemented in a variety of OCT systems and other systems in which signals from reference arm and sample arm can be interfered with one another to produce useful signals.

Exemplary Principle of Phase-Resolved Doppler FD-OCT

Exemplary Phase-resolved OCT techniques are described hereafter in the context of Fourier-Domain OCT, which is a category of OCT which is associated with the exemplary embodiments of the OFDI system according to the present invention. Fourier-Domain OCT can use an interference between two arms of an interferometer (e.g., a sample arm and a reference arm) to measure depth-dependent reflections in a turbid, semi-turbid and/or transparent medium. For example, an input light source is split into the reference arm and the sample arm. The light in the sample arm is directed to the sample to be imaged, and reflections from the sample are directed to a first port of an output coupler. The reference arm light is directed to the second port of the same output coupler. Spectral interference between the beams is measured by recording the interferometer output power as a function of wavelength. For a single reflection in the sample at position z where z denotes the total path-mismatch between the sample arm light and the reference arm light, the interferometer output can provided as follows:

$$S(k=2\pi/\lambda)\sim P(k)\sqrt{R(z)}\cos(k2z+\phi_z) \quad (1)$$

where S(k) is the output signal (optical power), P(k) is the source power at k, R(z) is the power reflectivity of the scatterer at position z, and ϕ_z is the phase of this reflection.

The reflectivity of the scatterer at position z is provided by the magnitude of the signal at frequency 2 kz. Typically, the detected signal is discretely sample, meaning that the measured signal is recorded in n discrete samples of the continuous output S(k). The discrete sampled output, S_1, is given by

$$S_l\sim P_l\sqrt{R(z)}\cos(k_l 2z+\phi_z),\ l=0\ldots(n-1) \quad (2)$$

where P_l is the source power at k_l. The discrete sampled output, S_1, is the discrete Fourier transformed ("DFT") to yield the complex reflectivity profile, a_i, as a function of depth index i,

$$a_i=DFT(S_l). \quad (3)$$

The signal from the scatter at position z is contained in the complex reflectivity profile coefficient a_m, where m is the depth index corresponding to position z. For example, each measurement of the discrete sampled output, S_l, can yield a single measurement of the complex reflectivity profile as a function of depth (A-line). The motion of the scatterer at depth index i results in a change in the phase, Φ_i, of the complex reflectivity profile coefficient a_i (Φ_i=angle(a_i)). If the complex reflectivity profile is provided with depth index i for A-line j as $a_{i,j}$, then a displacement of δ_z between A-lines j and j−1 can yield a phase change given by:

$$\Delta\phi_{i,j}=(\phi_{i,j}-\phi_{i,j-1})=2n<k>\delta_z. \quad (4)$$

The phase-resolved FD-OCT can measure motion in the scattering medium by calculating these phase differences at the sample depth for successive A-lines.

Phase-Resolved Doppler OFDI Technique

FD-OCT techniques of SD-OCT and OFDI systems and methods can both measure the discrete spectral interference S_l. However, these techniques generally differ in the implementation of this measurement. The OFDI systems and methods can use a wavelength-swept source and a single-element photoreceiver (and/or a set of single-element photoreceivers) to record S_l as a function of time. FIG. **1**A shows a block diagram of a exemplary embodiment of a high-speed OFDI technique for imaging at least a portion of a sample. The exemplary system shown in FIG. **1**A includes three modules **85**, **90** and **95**, e.g., a wavelength-swept source **85**, an interferometer **90**, and acquisition electronics arrangement **95**. The wavelength-swept source **85** (hereafter referred to as a swept source) can be provided as a ring-cavity laser. The swept source **85** can include a semiconductor optical amplifier ("SOA") **125** as a gain element and a polygon mirror filter **101**. The polygon mirror filter **101** can include a polygon mirror **100**, telescope **105**, diffraction grating **110**, and fiber collimator **113**. A polarization controller **120** may be included to optimize the laser polarization, and an output coupler **130** may provide a laser output. The output coupler nominally splits light equally between the output port **132** and laser port **131**. An optical circulator **115** directs light from the laser port **131** to the polygon mirror filter **101**, and directs light returning from the polygon mirror filter **101** to the polarization controller **120**. As the polygon mirror **100** rotates, the wavelength reflected from the polygon mirror filter **101** sweeps in wavelength, causing the laser output to sweep in wavelength in a similar manner.

The laser output at a port **132** can therefore be wavelength swept in time. This output is input to an interferometer which includes an interferometer coupler **135** which splits the light into a reference arm port **135***a* and sample arm port **135***b*. The reference arm light is split by a coupler **165**. The light from an output port **165***a* of the coupler **165** is directed to a second circulator **145** which passes the light to a fiber Bragg grating ("FBG") **150**. The FBG **150** has a narrowband reflection at a discrete wavelength within the wavelength-sweep range of the source. As the source **85** tunes past this reflection wavelength, a reflected optical pulse is generated. This pulse can be directed by a circulator **145** to a photoreceiver **155**, and such directed pulse is converted into a TTL pulse by a TTL pulse generator **160**. This TTL pulse can be used as a trigger signal for data acquisition electronics **200**. The light from another output port **165***b* of the coupler is directed to a third circulator **170** which directs the light to a variable optical delay **210**. This variable optical delay is used to path-match the interferometer **90**. The return light is directed by the circulator **170** to a polarization controller **175**, followed by a polarizer **180**, and finally to a first port **185***a* of an output coupler **185**. The sample arm light at the sample arm port **135***b* is directed to a fourth circulator **205**, which in turn directs the light on fiber **206** to the sample to be imaged. Imaging optics **215** can focus the light on the sample, and allow for a beam translation. The light reflected from the sample is collected by the same fiber **206**, and returned to the fourth circulator **205** which directs the light to a second port **185***b* of the output coupler **185**.

The reference arm light and the sample arm light interfere at the output coupler **185**. This interference signal is detected by a photoreceiver **190***a* on an output port **185***c* and a photoreceiver **190***b* on another output port **185***d*. The signals from these photoreceivers **190***a*, **190***b* are subtracted in a unit **195**, and directed toward an analog-to-digital (A-D) input port of a data acquisition (DAQ) board **200**.

The DAQ board **200** can acquires n samples at a clock rate f_{cl}, where n is predetermined. The clock signal can be internally generated in the DAQ board **200**. The trigger signal from the TTL pulse generator **160** may originate from the optical pulse produced by the FBG **150**. A lack of synchronization between the trigger pulse and the internal DAQ sample clock may cause a variable delay between the arrival of the trigger pulse and the first analog-to-digital conversion. This delay can be effected by one full sample clock period. Thus, if the sweep of the source is identified by $k_l=k_o+a_k l$, the sampled fringe for A-line j, $S_{l,j}$, can be given by

$$S_{l,j} \sim P_l\sqrt{R(z)}\cos((k_o+a_k(l+\Delta_j)2z+\phi_z),\ l=0\ \ldots\ (n-1) \tag{5}$$

where Δ_j can vary between 0 and 1 depending on the relative timing of the sample clock and the trigger pulse. The measured phase difference between successive A-lines for a stationary scatterer at position z can be given by:

$$\Delta\phi_{i,j}=a_k 2z(\Delta_j\Delta_{j-1}) \tag{6}$$

The phase difference results from timing variations in the acquisition time (described by Δ_j) and masks phase differences resulting from sample motion, degrading the system sensitivity. Writing the Nyquist limited making imaging depth as z_{Ny}=¶/($2a_k$) and using the normalized depth factor $\Gamma_z=z/z_{Ny}$, the timing-induced phase errors can be described by:

$$\Delta\phi_{i,j}<\Gamma_z\pi. \tag{7}$$

The above-described procedure in accordance with the present invention indicates that timing-induced phase errors increase linearly with depth up to, e.g., a maximum value of ¶ at $\Gamma_z=1$.

Correction of Timing-Induced Phase Errors through a Generation of a calibration Signal

According to one exemplary embodiment of the present invention, an additional signal can be generated by the exemplary system described herein and utilized to measure and subsequently correct for the timing-induced phase errors. For example, FIG. **2** shows an exemplary embodiment of such exemplary system in accordance with the present invention in which the sample arm is modified to facilitate the generation of the additional calibration signal. FIG. **2** shows that exemplary details of the sample arm which is after the optical circulator **205** illustrated in FIG. **1**. As shown in FIG. **2**, the light on a fiber **300** (i.e., the fiber **206** of FIG. **1**A) can be split by a coupler **305**. The light on a port **305***a* can be directed to a calibration mirror **310** that may have a variable optical delay. The light on a port **305***b* can be directed to the sample **320** in a similar manner to that of FIG. **1**A. The interferometer output signal forwarded from the calibration mirror can be localized in depth, and the variable optical delay may be adjusted such that it is located near the maximum imaging depth (and thus does not significantly obscure the image resulting from the sample optics **320**). The magnitude of the signal resulting from the variable optical delay can be adjusted such that it is significantly greater than that originating from the sample at that depth but not large enough such that significant auto-correlation noise is induced.

FIG. **3**A shows a graph **350** of an exemplary A-line resulting from the exemplary system configuration illustrated in FIG. **2**. A signal **360** from the calibration mirror is clearly seen among a sample (tissue) reflectance signal **355**. A flow diagram of an exemplary embodiment of a method for correcting the measured phase differences using this calibration mirror signal in accordance with the present invention is shown in FIG. **3**B, and provided as follows:

(1) Determine/calculate the DFT of each measured A-line, $a_{i,j}=\mathrm{DFT}(S_{i,j})$—step **370**.

(2) Determine/calculate an angle Φ_{ij}=unwrap(angle($a_{i,j}$)) where unwrap is a standard phase unwrapping algorithm which operates along the dimension j—step **375**.

(3) Determine/calculate a phase difference between adjacent A-lines $\Delta\Phi_{i,j}=\Phi_{i,j}-\Phi_{i,j}$—step **380**, and

(4) Determine/calculate a corrected phase difference, $\Delta\Phi'_{i,j}$, as $\Delta\Phi'_{i,j}=\Delta\Phi_{i,j}-(i/k)\Delta\Phi_{k,j}$, where k is a depth index of the calibration mirror signal—step **385**.

In a further embodiment, existing reflections from the optical probe are used as the calibration signal. FIG. **4** shows an exemplary embodiment of a distal-end optics portion of an exemplary OCT probe in accordance with the present invention. As shown in FIG. **4**, light may be transmitted on a fiber **400** to a collimating lens **410**, a right-angle prism **420**, and finally the light **430** exits the prism to the sample **440** to be imaged **440**. Discrete reflections can occur at any of the interfaces between the components, and the signal from these reflections can be utilized as a calibration signal in addition to and/or instead of the calibration mirror **310** of FIG. **2**.

In a further exemplary embodiment of the system according to the present invention shown in FIG. **6**, the calibration signal can be generated by a optical setup that may be external to an OFDI interferometer, and detected on a second detector that is sampled synchronously with the detector that samples the OFDI system output. In particular, a source **550** output can be split by a coupler **560** which directs a first portion of light to an OFDI interferometeric system **561** and a second portion of light to a calibration signal generator **562**. The OFDI interferometeric system **561** includes couplers **565** which provide signals to the reference arm and the sample arm, and the signal in the reference arm is forwarded to a coupler **575** which then forwarded a signal therefrom to a receiver **580**. In the sample arm, the signal is forwarded to another coupler **570**, which also receive the signal from the coupler **575**, and then provide a signal to a portion **585** of the sample **590**. The calibration signal generator **562** includes a periodic optical filter **595** which facilitates a generation of a intensity modulated optical signal, that is then detected at a receiver **596**. The periodic optical filter **595** can be, for example, a Fabry-perot etalon, a Mach-Zehnder interferometer, or a Michelson interferometer. The calibration signal and the OFDI signal may be detected on DAQ Channel 1 (shown as element **597**) and a DAQ channel 2 device (shown as element **598**), respectively. These channels can be sampled synchronously. Changes in acquisition timing may affect the phase of this calibration signal similarly to that described above when the calibration signal was generated with a mirror in the sample arm. Thus, the calibration signal detected on the DAQ channel 1 can be used to correct for timing-induced phase errors. Alternately or in addition, the calibration signal and the OFDI signal can be combined electronically, e.g., after the detection and before the analog-to-digital conversion, thus enabling both to be sampled by the same analog-to-digital channel.

In a further exemplary embodiment of the system according to the present invention which is shown in FIG. **15**, a balanced detection can be effectuated by balancing a signal channel that carries interference between the sample arm and the reference arm with a non-signal carrying reference path. As previously discussed, a source **900** can provide the electromagnetic radiation (e.g., a laser beam) to a polarization controller **905** may be included to optimize the laser polarization, and a fiber splitter **915** can receive the signal from the controller **905**. The fiber splitter **915** splits light to be forwarded to different paths. In one path, for example, a reference interference to calibrate the Doppler measurements can be generated in the non-signal carrying reference, e.g., by introducing a Fabry-Perot cavity **955** in the non-signal carrying reference (as indicated in the dashed box in FIG. **15**) which receives the radiation from the splitter **915**. The modulation depth on the reference as a function of wavelength as introduced by the Fabry-Perot cavity **955** should be small enough as to not affect the balanced detection scheme, and strong enough to provide a good calibration signal. Then, the cavity **955** forwards the resultant radiation to a variable attenuator, and then detected by balanced detectors D_1 and D_2 (**945**, **950**). In the other path, a polarization modulator or birefringent material **915** receives the split respective signal, and forwards it to a circulator **920** that directs one portion of the radiation to another fiber splitter **925** and splits the received signal to be forwarded to a sample arm and to a reference arm (and possibly to an optional polarizer **930**), and directs light returning therefrom to a polarization controller **935**, which then provides the polarized radiation to a polarization splitter **940** that also forwards the polarized split radiation to detectors D_1 and D_2 (**945**, **950**).

Correction of Timing-Induced Phase Errors through Post-Processing

In still another exemplary embodiment of the system, arrangement and method according to the present invention, phase measurements can be corrected without the use of a calibration mirror. In this exemplary technique, a intensity-weighted linear fit can be applied to each measured phase difference line, $\Delta\Phi_{i,j}$, as a function of depth index i, $y_{i,j}=m_j i+b_j$. The corrected phase differences can be given by $\Delta\phi_{i,j}=\Delta\phi_{i,j}-m_j i-b_j$.

Correction of Timing-Induced Phase Errors through the Improved Acquisition/Source Synchronization

In a further embodiment, the timing-induced phase errors are reduced by improving the synchronization between the swept source and the DAQ board. The rotational speed of the polygon mirror **100** of FIG. **1**A can be determined by the frequency of a signal input to the polygon mirror driver (not shown). If such signal is generated from the same clock as the one which generates the sample clock of the DAQ board, and the polygon mirror driver can maintain adequate phase-locking between the polygon and drive signal, then the synchronization between the wavelength-sweep and the data acquisition can be achieved. In this case, the delay of Eq. 5 denoted by Δ_j can remain constant, and thus the timing-induced phase errors may be reduced.

In a still further exemplary embodiment of the system according to the present invention that is shown in FIG. **7**, an acquisition sample clock can be generated optically by using a periodic filter such as a Fabry-Perot etalon, a Mach-Zehnder interferometer, and/or a Michelson interferometer. As shown in FIG. **7**, a portion of a swept source **600** can be directed to a sample clock generator **606** which can include a periodic optical filter **610**, a receiver **615** and a TTL generating circuit **620**. The periodic optical filter **610** can produce an oscillating output signal which is detected at the receiver **615**. The receiver output is directed to the TTL generating circuit **620** which can include voltage comparators and/or Schmitt triggers to generate a TTL pulse train. This pulse train can be input into a DAQ external sample clock input port **655** to be used as a sample clock. Because sampling can be synchronized to the laser wavelength sweep through the sample clock generator, the timing-induced noise can be reduced directly. This technique can be used separately or in combination with previously described techniques for correcting phase errors.

Applications of Phase-Resolved OFDI

In still another exemplary embodiment of the present invention, the phase-resolved OFDI system can be used to image blood flow distributions during an intravascular OFDI imaging. An exemplary device capable of imaging blood flow is shown in FIG. **5**. For example, an exemplary optical probe **510** in accordance with the present invention can be placed inside an artery **520**, and the imaging beam **500** can be emitted from a side of the probe **510**. The depth resolved blood flow can be detected, and if the probe is rotated, a 2D map of the blood flow may be created. The end view illustrates the rotation of the imaging beam. Alternately, a forward looking probe can be provided for imaging the blood ahead of the probe **510**.

In yet another exemplary embodiment of a phase-resolved OFDI system of the present invention which is shown in FIG. **8**, a frequency shifter can be provided therein. For example, a frequency shifter **711** can be used to enable a doubling of the imaging depth. If the frequency shifter **711** is driven with a signal that is unsynchronized with the sampling clock, noise in the measured phase may result. In the exemplary embodiment of the system shown in FIG. **8**, the frequency shifter is driven with a signal derived from the sample clock. Light is output from the source and split into a reference arm and a sample arm by the first splitter **710**. The reference arm contains a frequency shifter **712** and the sample arm contains the same frequency shifter **711**. Generally, only one of the frequency shifters **711**, **712** can be actively driven, and the other one of the shifters **711**, **712** may be used to compensate for the dispersion of the driven frequency shifter. The frequency shifter that is not driven can alternatively be a dispersion compensating element. The frequency shifter **712** in the reference arm may be driven through a signal carried on line **713** which can be derived from a DAQ sample clock output **725**. This output clock **725** may be down-shifted in frequency using a "Divide by N" digital logic circuit **720**, and the resulting signal can pass through an amplifier and filter stage **715** to produce a single tone on line **713**. Because the drive signal for the frequency shifter may be driven by the DAQ sample clock output **725**, the phase of the frequency shift may be synchronous with the sample clock, and thus does not necessarily induce additional phase noise. Various exemplary techniques in accordance with the present invention described herein can be used to correct for any residual timing-induced noise.

In a further exemplary embodiment of the phase-resolved OFDI system of the present invention, such system can be used to determine variations in the optical-path length between two points in depth as a function of time. For example, FIG. **9** illustrates an illustration of an exemplary use of the exemplary embodiment of the phase-resolved OFDI system to measure depth-resolved changes in optical path length as a function of time. This use is provided for the case of a object between a first reflective surface **805** at depth **z1** and a second reflective surface **810** at depth **z2**. Between the reflective surfaces **805**, **810** is an object to be imaged **815**. The reflective surfaces **805**, **810** can either be fixed external surfaces such as glass slides or structural features of the biological object itself. By monitoring the phase of the signals due to the reflections off these surfaces **805**, **810**, the optical path length between **z1** and **z2** can be monitored, allowing changes in the object to be monitored. These potential changes can include variations in the object index of refraction with time, or expansion of the object in time. In the illustration of FIG. **9**, the imaging beam can be held stationary, and used to monitor changes at a fixed transverse point over time.

A further exemplary illustration of an exemplary use of the exemplary embodiment of the phase-resolved OFDI system to measure depth-resolved changes in an optical path length as a function of transverse displacement. An imaging beam **850** is directed toward a sample object located between a first reflective surface **855** and a second reflective surface **865**. The optical path length difference between these reflective surfaces **855**, **865** is known by the design of the system and/or a prior measurement before an object **860** is inserted. The phase of the reflective surfaces **855**, **865** can be measured as a function of a transverse displacement of the imaging beam **850**, and the variations in the transverse optical path length of the object **860** can be found by comparing the phase difference between the two signals with the phase difference as measured and/or known previously without the object being present. For example, if the system is has enough stability, the first surface reflectance at z**1** may not be needed.

It can be appreciated by those skilled in the art that one of the embodiments can be used in combination with other exemplary embodiments described herein to provide various phase-resolved OFDI systems with reduced timing-induced phase noise in accordance with the present invention.

EXAMPLE

The exemplary embodiment(s) of the system, apparatus and method according to the present invention have been verified as follows:

The phase differences between successive A-lines were measured in the exemplary configuration of FIG. **2** with a stationary sample mirror in the sample arm. FIG. **11** an exemplary graph **1010** of measured differential phases for the calibration mirror and a stationary mirror in the sample arm before and after a correction for timing-induced phase errors according to an exemplary embodiment of the present invention. The calibration mirror signal **1015** and the uncorrected sample signal **1020** show phase errors of the magnitude predicted by Eq. 7. The corrected phase measurements **1025** show substantial reduction in spurious phase differences.

FIG. **12** shows an illustration of measurements taken of Intralipid (scattering liquid) flow through a tube immersed in the same stationary Intralipid. Both the OFDI intensity image **1030** and the flow image **1035** are shown. The presence of flow is clearly detected by the phase-resolved OFDI system of an exemplary embodiment of the present invention.

FIGS. **13A-13C** show illustrations of a measurement of Intralipid flow through a tube in which the flow rate is large enough that phase differences greater than if are induced. In the graph of FIG. **13**A, the depth resolved flow **1040** as a function of time is plotted. In the graph of FIG. **13**B, the measured phase differences **1045** are unwrapped to remove discontinuities of 2π such that the large flow profile can be measured. FIG. **13**C shows the graph of the unwrapped flow profile **1050** at time T as marked in FIGS. **13**(*a*) and **13**(*b*). This shows the ability of phase-resolved OFDI to measure large flow rates that induced phase differences greater than π without the deleterious effects of fringe washout.

FIG. **14** shows an illustration of a phase-resolved measurement of blood flow in vivo near the nail bed of a human finger. Vessels are clearly shown in the flow image **1055** that do not appear in the intensity image **1060**.

The foregoing merely illustrates the principles of the invention. Various modifications and alterations to the described embodiments will be apparent to those skilled in the art in view of the teachings herein. Indeed, the arrangements, systems and methods according to the exemplary embodiments of the present invention can be used with and/or implement any OCT system, OFDI system, SD-OCT system or other imaging systems, and for example with those described in International Patent Application PCT/US2004/029148, filed Sep. 8, 2004 which published as International Patent Publication No. WO 2005/047813 on May 26, 2005, U.S. patent application Ser. No. 11/266,779, filed Nov. 2, 2005 which published as U.S. Patent Publication No. 2006/0093276 on May 4, 2006, and U.S. patent application Ser. No. 10/501,276, filed Jul. 9, 2004 which published as U.S. Patent Publication No. 20050018201 on Jan. 27, 2005, the disclosures of which are incorporated by reference herein in their entireties. It will thus be appreciated that those skilled in the art will be able to devise numerous systems, arrangements and methods which, although not explicitly shown or described herein, embody the principles of the invention and are thus within the spirit and scope of the present invention. In addition, to the extent that the prior art knowledge has not been explicitly incorporated by reference herein above, it is explicitly being incorporated herein in its entirety. All publications referenced herein above are incorporated herein by reference in their entireties.

What is claimed is:

1. An apparatus comprising:

at least one hardware first arrangement including a source which provides a radiation which includes at least one first electro-magnetic radiation directed to a sample and at least one second electro-magnetic radiation directed to a reference, wherein a frequency of the radiation provided by the at least one first arrangement varies over time; and

at least one hardware second arrangement which includes a detector that detects a particular interference signal between at least one third radiation associated with the at least one first radiation and at least one fourth radiation associated with the at least one second radiation,

wherein that particular interference signal is detected by the detector across a first radiation frequency range,

wherein the at least one second arrangement obtains at least one first phase of at least one frequency component of the particular interference signal, and wherein the at least one second arrangement includes a hardware computing arrangement which compares the at least one first phase with at least one second phase of at least one frequency component of a previously-detected interference signal which is detected by the detector across a second radiation frequency range, and

wherein the hardware computing arrangement generates at least one image of at least one portion of the sample that substantially excludes information caused by a difference between the first and second radiation frequency ranges based on the comparison and as function of the interference signals.

2. The apparatus according to claim **1**, wherein the at least one second arrangement is configured to determine a signal associated with at least one further phase of at least one further frequency component of a further interference signal, and wherein the at least one second phase is associated with the signal.

3. The apparatus according to claim **1**,

wherein the at least one second arrangement is configured to determine a signal associated with at least one further phase of a further interference signal, the further interference signal being different from the particular and previously-detected interferences.

4. The apparatus according to claim **3**, wherein the at least one second arrangement obtains the particular and previously-detected interference signals at different times.

5. The apparatus according to claim **3**, wherein the at least one second arrangement obtains the particular and previously-detected interference signals at different locations of the sample.

6. The apparatus according to claim **1**, comprising a further reference configure to receive at least one portion of the radiation and provide a further radiation so as to generate a signal, wherein at least one of the signal or the at least second phase is associated with the further radiation.

7. The apparatus according to claim **6**, wherein the at least one second arrangement is configured to calibrate the at least one first phase based on the signal.

8. The apparatus according to claim **7**, wherein the calibration is based on at least one of an actual distance or an optical distance between the sample and the first arrangement.

9. The apparatus according to claim **1**, wherein the at least one second arrangement is configured to calibrate the signal based on at least one of an actual distance or an optical distance between the sample and the first arrangement.

10. The apparatus according to claim **1**, further comprising:

at least one hardware third arrangement including a further reference which receives at least one portion of the radiation and provides a further radiation which is at least partially based on the radiation, wherein the hardware computing arrangement induces a phase shift of the particular phase based on the further radiation, and wherein the further radiation is independent of any property of the sample.

11. The apparatus according to claim **10**, wherein the at least one hardware third arrangement is provided in the sample arm.

12. The method according to claim **10**, wherein the reference includes a mirror that is positioned to directly reflect the at least one portion to the at least one second arrangement.

13. The apparatus according to claim **10**, wherein the further radiation is distinct from the at least one second radiation and the at least one fourth radiation.

14. The apparatus according to claim **10**, wherein the at least one first arrangement includes a single laser source which generates the radiation.

15. The apparatus according to claim **10**, wherein the computing arrangement induces the phase shift at least one of digitally or mathematically.

16. The apparatus according to claim **1**, wherein the at least one second arrangement detects a further signal corresponding to a further interference signal between the at least one second and third radiations, and wherein the further signal is associated with at least one phase of at least one frequency component of an additional interference associated with the further signal.

17. The apparatus according to claim **1**, wherein the at least one second arrangement determines image information based on the comparison between the first and second phases.

18. A method comprising:

providing a radiation which includes at least one first electro-magnetic radiation directed to a sample and at least one second electro-magnetic radiation directed to a reference, wherein a frequency of the radiation varies over time;

detecting a particular interference signal between at least one third radiation associated with the at least one first radiation and at least one fourth radiation associated with the at least one second radiation, wherein the particular interference signal is detected across a first radiation frequency range;

obtaining at least one first phase of at least one frequency component of the particular interference signal; and

with a hardware computer arrangement, comparing the at least one first phase with at least one second phase of at least one frequency component of a previously-detected interference signal which is detected by across a second radiation frequency range, and

with the hardware computer arrangement, generating at least one image of at least one portion of the sample that substantially excludes information caused by a difference between the first and second radiation frequency ranges based on the comparison and as function of the interference signals.

19. The method according to claim **18**, further comprising determining a signal associated with at least one further phase of a further interference signal, the further interference signal being different from the particular and previously-detected interference signals.

20. The method according to claim **18**, further comprising:

determining a signal associated with at least one further phase of a further interference signal, the further interference signal being different from the particular and previously-detected interference signals.

21. The method according to claim **20**, further comprising obtaining the particular and previously-detected interference signals at different times.

22. The method according to claim **20**, further comprising obtaining the particular and previously-detected interference signals at different locations of the sample.

23. The method according to claim **18**, further comprising:

receiving at least one portion of the radiation and provide a further radiation so as to generate a signal, wherein at least one of the signal or the at least second phase is associated with the further radiation.

24. The method according to claim **23**, further comprising:

calibrating the at least one first phase based on the signal.

25. The method according to claim **24**, wherein the calibration is based on at least one of an actual distance or an optical distance between the sample and a particular arrangement.

26. The method according to claim **18**, further comprising:

calibrating the second signal based on at least one of an actual distance or an optical distance between the sample and a particular arrangement.

27. The method according to claim **18**, further comprising:

receiving at least one portion of the radiation and provide a further radiation which is at least partially based on the radiation; and

inducing a phase shift of the particular phase based on the further radiation, and wherein the further radiation is independent of any property of the sample.

28. The method according to claim **27**, wherein the at least one portion of the radiation is received in the sample arm.

29. The method according to claim **27**, wherein the further radiation is distinct from the at least one second radiation and the at least one fourth radiation.

30. The method according to claim **27**, wherein the radiation is generated by a single laser source.

31. The method according to claim **27**, wherein the phase shift is induced at least one of digitally or mathematically.

32. The method according to claim **18**, further comprising detecting a further signal corresponding to a further interference signal between the at least one second and third radiations, and wherein the signal is associated with at least one phase of at least one frequency component of an additional interference signal associated with the further signal.

33. The method according to claim **18**, further comprising imaging information based on the comparison between the first and second phases.

34. A system comprising:

at least one hardware first arrangement including a detector which detects an interference signal between at least one first radiation associated with a first split portion of a radiation received from a sample and a second split portion of the radiation received from a reference, wherein a frequency of the radiation varies over time, wherein the interference signal is detected by the detector across a first radiation frequency range, wherein the at least one arrangement obtains at least one first phase of at least one frequency component of the interference signal, wherein the at least one detector arrangement includes a one hardware computing second arrangement which compares the at least one first phase with at least one second phase of at least one frequency component of a previously-detected interference signal which is detected by the detector across a second radiation frequency range, and wherein the one hardware computing second arrangement generates at least one image of at least one portion of the sample that substantially excludes information caused by a difference between the first and second radiation frequency ranges based on the comparison and as function of the interference signals.

35. The apparatus according to claim **34**, wherein the at least one hardware first arrangement detects a further signal corresponding to a further interference signal between the first and second split portions of the radiation, and wherein the previously-detected interference signal is associated with at least one phase of at least one frequency component of an interference signal associated with the further signal.

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